MEDICAL PROCEEDINGS

MEDIESE BYDRAES

A South African Journal for the Advancement of Medical Science

'n Suid-Afrikaanse Tydskrif vir die Bevordering van die Geneeskunde

P.O. Box 1010 · Johannesburg | Posbus 1010 · Johannesburg

Vol. 4 | 28 Junie 1958 June 28 | No. 13

REDAKSIONEEL · EDITORIAL

SKF LABORATORIES SE BEURS VIR NA-GRAADSE KLINIESE STUDIE IN SUID-AFRIKA

Hierdie beurs is moontlik gemaak deur 'n toelae wat deur SKF Laboratories (Pty.) Limited, Posbus 784, Port Elizabeth, beskikbaar gestel is. Die genoemde firma is die Suid-Afrikaanse tak van Smith, Kline and French Laboratories Ltd., Londen.

Die Keurkomitee ('n volkome onafhanklike raad van mediese praktisyns) bestaan uit die volgende:

Prof. J. F. Brock (Kaapstad);
Prof. G. A. Elliott (Johannesburg);
Dr. H. A. Shapiro (*Ere-Voorsitter,* Johannesburg);
Dr. M. Shapiro (Johannesburg);
Dr. M. M. Suzman (Johannesburg);
Prof. H. W. Snyman (Pretoria).

Aansoeke word ingewag van geregistreerde *algemene praktisyns* wat ten minste 7 jaar lank aktief in Suid-Afrika gepraktiseer het.

Die Beurs is bedoel vir na-graadse kliniese studie en nie vir mediese navorsing nie. Dit is beskikbaar vir 'n tydperk van ten minste 2 maande aan enige Mediese Skool in Suid-Afrika.

Die totale waarde van die beurs is £200.

Die kandidaat moet 'n kort uiteensetting van sy voorgestelde studiekursus verstrek, en hy moet aandui by watter inrigting hy hierdie kursus wil loop.

Geen geld sal aan die suksesvolle aansoeker uitbetaal word nie totdat hy die Keurkomitee tevrede gestel het dat hy aangeneem is vir die

SKF LABORATORIES AWARD FOR POST-GRADUATE CLINICAL STUDY IN SOUTH AFRICA

This award has been established by a grant from SKF Laboratories (Pty.) Limited, P.O. Box 784, Port Elizabeth. This is the South African branch of Smith, Kline and French Laboratories Ltd., London.

The Selection Committee (an entirely independent board of medical practitioners) consists of the following:

Prof. J. F. Brock (Cape Town);
Prof. G. A. Elliott (Johannesburg);
Dr. H. A. Shapiro (*Honorary Chairman,* Johannesburg);
Dr. M. Shapiro (Johannesburg);
Dr. M. M. Suzman (Johannesburg);
Prof. H. W. Snyman (Pretoria).

Applications are invited from registered *general practitioners* who have been in active practice in South Africa for at least 7 years.

The Bursary is intended for post-graduate clinical study and not for medical research. It is available for not less than a 2-month period at any Medical School in South Africa.

The total value of the Bursary is £200.

The candidate must submit a brief statement of his proposed course of study and indicate the institution at which he intends to undertake it.

No payments will be disbursed to the successful applicant until he has satisfied the Selection Committee that he has been accepted for the period of post-graduate study at a South African Medical School.

tydperk van na-graadse studie aan 'n Suid-Afrikaanse Mediese Skool.

Aansoek moet gedoen word op die voorgeskrewe vorm wat verkrygbaar is van:

Dr. H. A. Shapiro (*Ere-Voorsitter*), Keurkomitee, SKF Laboratories se Beurs vir Na-Graadse Kliniese Studie, Posbus 1010, Johannesburg.

Die sluitingsdatum vir aansoeke is 16 Augustus 1958.

Applications must be made on the prescribed form which is obtainable from:

Dr. H. A. Shapiro (Honorary Chairman), Selection Committee, SKF Laboratories Award for Post-Graduate Clinical Study, P.O. Box 1010, Johannesburg.

Closing date for applications: 16 August 1958.

LIPO-PROTEÏENFRAKSIES EN KORONÊRE SLAGAARKWAAL

Die groot aantal menselewens wat gedurende die afgelope dekades deur koronêre hartkwaal opgeëis is, het aktiewe ondersoek aangewakker na die oorsake van aterosklerose, veral vir sover dit bloedvoorsiening aan die hart betref.

Marks[1] het onlangs 'n opname gemaak van die verwantskap tussen liggaamsgewig en mortaliteit en morbiditeit. Hy beklemtoon dan ook wat lank reeds 'n kliniese aksioom is, nl. dat 'n te groot gewig (selfs in 'n betreklik geringe mate) skadelik is, en grotendeels weerspieël word onder meer deur die frekwensie van sterfgevalle ten gevolge van hartkwaal.

Dit is hierdie besef van die belangrikheid van vetsug wat die aandag pertinent gevestig het nie alleen op dieetvet in die algemeen nie, maar ook op onversadigde vetsure in besonder.[2]

Interessante lig is ook op die etiologiese probleem gewerp deur vergelykende studies, bv. die seldsaamheid van sterfgevalle ten gevolge van koronêre hartkwaal onder die Suid-Afrikaanse naturelle. Op een tydstip is daar gemeen dat dit verduidelik kan word op grondslag van 'n verskillende anatomiese patroon in die koronêre slagaarboom.[3] Dit skyn egter asof daar maar bra min ondersteuning vir hierdie mening is. Aan die ander kant het die opvallend verskillende voedselgewoontes van die naturel die aandag gevestig op die een of ander dieetfaktor as 'n belangrike oorsaaklike faktor by die totstandbrenging of voorkoming van die patologiese letsel in die bloedvate van die hart.

Dit is interessant en miskien betekenisvol dat hoewel Laurie en Woods[4] onlangs die Suid-Afrikaanse naturel se betreklike immuniteit teen aterosklerose in twyfel getrek het, hul waarnemings beperk gebly het tot die aorta en die serebrale vate. Hoewel hulle feitlik geen

1. Marks, H. H. (1957): Metabolism, **6**, 423.
2. Bronte-Stewart, Keys, A., Brock, J. F., Moodie, A. D., Keys, M. H. en Antonis, A. (1955): Lancet, **2**, 103.
3. Brink, A. J. (1949): Clin. Proc., **8**, 137.
4. Laurie, W. en Woods, J. D. (1958): Lancet, **1**, 231.

LIPO-PROTEIN FRACTIONS AND CORONARY ARTERY DISEASE

In recent decades an appreciation of the grave toll taken by coronary heart disease has stimulated active investigations into the causes of atherosclerosis, particularly as it affects the blood supply of the heart.

Marks[1] recently surveyed the relationship of body weight to mortality and morbidity. He emphasized, what has long been a clinical axiom, that overweight (even of relatively mild degree) is harmful and is largely reflected, *inter alia*, in the frequency of death from heart disease.

It is this appreciation of the importance of obesity which has focused attention, not only on dietary fat in general, but on the unsaturated fatty acids in particular.[2]

Interesting light has also been thrown on the aetiological problem by comparative studies, e.g. the rarity of death from coronary heart disease in the South African Bantu. At one time it was thought that this might be explained on the basis of a different anatomical pattern in the coronary artery tree.[3] Little support seems to have been forthcoming for this view. On the other hand, the markedly different food habits of the Bantu centred attention on some dietary factor as an important causal agent in producing or preventing the pathological lesion in the blood vessels of the heart.

It is interesting, and perhaps significant, that although Laurie and Woods[4] recently challenged the relative immunity of the South African Bantu to atherosclerosis, their observations were confined to the aorta and the cerebral vessels. Although they found virtually no difference between the incidence of atherosclerosis (in particular in cerebral vascular disease) in White and non-White populations in South Africa, their communication significantly fails

1. Marks, H. H. (1957): Metabolism, **6**, 423.
2. Bronte-Stewart, B., Keys, A., Brock, J. F., Moodie, A. D., Keys, M. H. and Antonis, A. (1955): Lancet, **2**, 103.
3. Brink, A. J. (1949): Clin. Proc., **8**, 137.
4. Laurie, W. and Woods, J. D. (1958): Lancet, **1**, 231.

verskil tussen die voorkoms van aterosklerose (in besonder in gevalle van serebrale vaatkwale) by die blanke en die nie-blanke bevolking van Suid-Afrika aangetref het nie, is dit betekenisvol dat hul mededeling nie die seldsaamheid van koronêre hartkwaal onder die naturelle enigsins in twyfel trek nie.

Die moontlike verwantskap tussen die dieet en die ontstaan van koronêre trombose kan onder 4 opskrifte bespreek word:

1. Die vetinhoud van die dieet.
2. Die vervoer van vet deur die bloed en die metabolisme daarvan in die weefsels.

Dit is op hierdie stadium dat die belangrikheid van die lipo-proteïenpatroon en sy *alfa-* en *beta*-fraksies geëvalueer moet word. Hulle kan 'n belangrike rol in die werklike metabolisme van vet speel.

3. Die ontwikkeling van aterosklerose. Dit opper die vraag of daar enige oorsaaklike verband tussen (2) en (3) is.
4. Die plek en meganisme van trombose as dit by die letsel van aterosklerose gevoeg word.

Die skakels tussen (1) en (2) of (2) en (3) of (3) en (4) word nog nie duidelik begryp nie. Dit sou derhalwe foutief wees om sommer aan te neem dat daar 'n belangrike of selfs 'n noodsaaklike verband tussen (1) en (4) is, behalwe miskien op 'n baie breë en algemene grondslag.*

Elders in hierdie uitgawe publiseer ons 'n belangrike mededeling deur Bloomberg wat die aandag op die plasma-lipo-proteïenpatroon, en op die betreklike verhoudinge van sy *alfa-* en *beta*-fraksies vestig. Bloomberg se werk bevestig die resultate van ander Suid-Afrikaanse navorsers[2, 5] en dui daarop dat die normale Suid-Afrikaanse naturel van die Suid-Afrikaanse blanke verskil wat lipo-proteïenpatroon sowel as die totale serumcholesterol betref. Stedelike naturelle het hoër *alfa-* en laer *beta*-lipo-proteïencholesterols as blankes. Jong plattelandse naturelle het laer *alfa*-lipo-proteïencholesterols as jong stedelike naturelle, en albei het laer *beta*-lipo-proteïencholesterols as ou stedelike naturelle.[6]

* O'Brien[10] het onlangs die stollingstyd volgens talle metodes gemeet by pasiënte wat aan koronêre trombose ly. Die kontrolegroep was gesonde mans van dieselfde ouderdom (40–60 jaar). Hy kon geen getuienis vind om die mening te staaf dat hiperkoagulasievermoë na 'n maaltyd verantwoordelik is vir die beweerde verband tussen die vetinhoud van die dieet en koronêre trombose nie.

Die probleem van stolling *in vivo* is egter besonder ingewikkeld. Die moontlike rol van sirkulerende fibrienolisien[11] wag, byvoorbeeld, nog op evaluasie.

5. Walker, A. R. P. en Bersohn, I. (1957): *Medicine in South Africa,* bl. 106. Bylae tot S.A. Tyd. vir Genees.
6. Bloomberg, B. (1958): Circulation (*in die pers*).

to challenge the rarity of coronary heart disease in the Bantu.

The possible relationship between the diet and the development of coronary thrombosis may be discussed under 4 headings:

1. The fat content of the diet.
2. Fat transport in the blood and its metabolism in the tissues.

It is at this stage that the importance of the lipo-protein pattern and its *alpha* and *beta* fractions must be assessed. These may play an important role in the actual metabolism of fat.

3. The development of atherosclerosis. This raises the problem whether there is any causal connexion between (2) and (3).
4. The site and mechanism of thrombosis superimposed on the lesion of atherosclerosis.

The links between (1) and (2) or (2) and (3) or (3) and (4) are not yet clearly understood. It is therefore fallacious to jump to the conclusion that there is a major or even a necessary link between (1) and (4), except in a very broad and general way.*

Elsewhere in this issue, we publish an important communication by Bloomberg which draws attention to the plasma lipo-protein pattern, and the relative proportion of its *alpha* and *beta* fractions. Bloomberg's work confirms the results of other South African investigators[2, 5] and indicates that normal South African Bantu differ from South African Whites in lipo-protein pattern as well as in total serum cholesterol. Urban Bantu have higher *alpha-* and lower *beta*-lipo-protein cholesterols than have Whites. Young rural Bantu have lower *alpha*-lipo-protein cholesterols than have young urban Bantu, and both have lower *beta*-lipo-protein cholesterols than have old urban Bantu.[6]

These differences are thought to be of significance in defining the 'ideal' values of both cholesterol fractions. Studies in Whites (as Bloomberg shows in this issue) reveal that although high cholesterol levels are associated with coronary thrombosis, the wide ranges and overlapping of the values of all the lipid frac-

* O'Brien[10] has recently measured the clotting time by many methods in subjects with coronary thrombosis, the controls being healthy men of similar age (40–60 years). He was unable to find any evidence to support the view that postprandial hypercoagulability is responsible for the alleged connexion between the fat content of the diet and coronary thrombosis.

The problem of clotting *in vivo* is, however, extremely complex, e.g. the possible role of circulating fibrinolysin[11] awaits evaluation.

5. Walker, A. R. P. and Bersohn, I. (1957): *Medicine in South Africa,* p. 106. Supp. S. Afr. Med. J.
6. Bloomberg, B. (1958): Circulation (*In the press*).

Daar word gemeen dat hierdie verskille van betekenis is by die omskrywing van die ‚ideale' waarde van albei cholesterol-fraksies. Die studies wat met blankes gedoen is (soos Bloomberg in hierdie uitgawe aantoon) openbaar dat hoewel hoë cholesterolpeile met koronêre trombose geassosieer is, die breë bestek en oorvleueling van die waarde van alle lipied-fraksies dit nogal gevaarlik vir die klinis maak om die individuele pasiënt se vatbaarheid vir die siekte te antisipeer. Daar is tans ruimskootse bewyse dat 'n kandidaat vir 'n koronêre ramp nie deur bloed-lipo-proteïenstudies aangewys kan word nie.[7, 8] Bloomberg se waarnemings kan egter van betekenis wees by die aanduiding van maatreëls om die ernstige gevolge van koronêre kwaal onder beskaafde lewenstoestande in baie dele van die wêreld te stuit. Dit is moontlik dat die besondere fraksionele lipo-proteïenpatroon van die naturel hom teen die ontstaan van koronêre slagaarkwaal beskerm.

Hierdie benadering is veral van belang met die oog op die bewys dat 'n dieet met 'n lae vetinhoud biologies ongesond is.[9] 'n Meer rasionele profilaktiese benadering in die lig van die bestaande inligting is miskien om die aandag te vestig op die verskillende maniere waarop die fraksionele lipoproteïenpatroon deur dieet, hormone of andersins gekontroleer kan word. Ons metaboliese doelwit kan bes moontlik die lipiedpatroon wees wat so kensketsend van die jong stedelike naturel is.

ANTI-POLIOMIËLITISMAATREËLS IN SUID-AFRIKA

Die koms van die winter benadruk die noodsaaklikheid van 'n aggressiewe veldtog om die bevolking te immuniseer teen die paralitiese gevare van poliomiëlitis wat altyd hul hoogtepunt gedurende die somermaande bereik. Daar word tans natuurlik vrywel allerweë aangeneem dat daar geen rede is waarom inenting, selfs gedurende 'n epidermie, vermy hoef te word nie; maar as daar die volste gebruik gemaak word van die seisoene tussen die somerhoogtepunte, sal die ingeënte bevolking voldoende tyd kry om die maksimum-immuniteit wat deur die geïnaktiweerde entstof verleen word, op te bou.

In hierdie land is ons verbind tot 'n grootskeepse voorkomingsbeleid ten opsigte van poliomiëlitis. 'n Geïnaktiweerde entstof word plaaslik vervaardig, en oorsese fabrikante is tans ook in staat om 'n entstof van die Salk-tipe uit hul aansienlike voorrade aan Suid-Afrika te verskaf. Hierdie toestand gee die praktisyn sowel as die pasiënt 'n groter keuse wat entstowwe betref. Dit behoort ook te

7. *Report on Liproprotein and Atherosclerosis of the National Advisory Heart Council* (1956): Circulation, **14,** 691.
8. Lawry, E. Y. *et al.* (1957): Amer. J. Med., **22,** 605.
9. Kinsell, L. W. *et al.* (1958): Lancet, **1,** 334.
10. O'Brien, J. R. (1958): Lancet, **1,** 410.
11. Greig, H. B. W. (1956): Lancet, **2,** 16.

tions make it hazardous for the clinician to anticipate the individual patient's liability to the disease. There is now ample evidence that blood lipo-protein studies cannot predict the candidate for coronary catastrophe.[7, 8] Bloomberg's observations, however, may be significant in pointing to measures which may reverse the serious consequences of coronary disease under civilized conditions of living in many parts of the world. It is possible that the particular fractional lipo-protein pattern of the Bantu may protect against the development of coronary artery disease.

This approach is particularly important in view of the evidence that a low fat diet is biologically unsound.[9] A more rational prophylactic approach in the light of existing information is perhaps to focus attention on the various ways in which the fractional lipo-protein pattern may be controlled, whether by dietary, hormonal or other means. Our metabolic objective may well need to be the lipid pattern characteristic of the young urban Bantu.

ANTI-POLIOMYELITIS MEASURES IN SOUTH AFRICA

The advent of the winter months emphasizes the need for an aggressive campaign to immunize the population against the paralytic hazards of poliomyelitis which invariably reach their height in the summer months. It is by now, of course, fairly well established that there is no reason to refrain from inoculation, even during an epidemic; but if full use is made of the seasonal interval between the summer peaks, the inoculated population will have time to build up the maximal degree of immunity which can be conferred by the inactivated vaccine.

In this country we are committed to a full-scale preventive policy in respect of poliomyelitis. An inactivated vaccine is made locally, and overseas manufacturers are now also in a position to supply the South African market with a Salk-type vaccine from their very considerable resources. This situation increases the freedom of choice of vaccine both for the medical practitioner and the patient. It should also ensure a continuous and steady sup-

7. *Report on Lipoprotein and Atherosclerosis of the National Advisory Heart Council* (1956): Circulation, **14,** 691.
8. Lawry, E. Y. *et al.* (1957): Amer. J. Med., **22,** 605.
9. Kinsell, L. W. *et al.* (1958): Lancet, **1,** 334.
10. O'Brien, J. R. (1958): Lancet, **1,** 410.
11. Greig, H. B. W. (1956): Lancet, **2,** 16.

verseker dat daar 'n voldoende en ononderbroke voorraad is op enige tydstip wanneer die entstof benodig word.

Die geslaagde vervaardiging van poliomiëlitisentstof gaan onvermydelik met moeilikhede en onsekerheid gepaard, en die Suid-Afrikaanse vervaardigers het reeds te kampe gehad met al die wisselvallighede wat deur die massaproduksie van hierdie entstof opgelewer word. Op een tydstip het plaaslike voorrade so ver agtergeraak dat 300,000 dosisse uit die Verenigde State ingevoer moes word—'n verstandige stap wat die algehele goedkeuring van die mediese professie in die Unie weggedra het.

Die is egter verontrustend om te verneem dat die verspreiding van die voorraad ingevoerde entstof wat teen die begin van April van vandeesjaar in hierdie land aangekom het, meer as 2 maande lank vertraag is. Gedeeltelik moet dit toegeskryf word aan administratiewe draaiery solank die owerheid die toestand oorweeg het—'n uiters betreurenswaardige gebeurtenis. Poliomiëlitisentstof het 'n nuttigheidsvervaldatum wat 6 maande ná verpakking in werking tree. Die tempo waarteen voorrade ingevoerde entstof deur die lisensie-owerheid afgehandel word, sal derhalwe aansienlik bespoedig moet word, veral met die oog op die feit dat enige toetse wat die owerheid besluit om toe te pas, baie tydrowend kan wees. Aangesien die entstof 'n betreklik kort lewensduur het, behoort enige protokol of ander komitee wat raad aan die Minister oor sodanige sake gee, in staat te wees om sonder versuim te vergader sodat alle groepe polio-entstof sonder die minste versuim beskikbaar gestel kan word. Dit is nie in die beste belang van 'n program vir die beveiliging van openbare gesondheid dat daar enige vermybare vertraging met die klaring van entstof moet wees nie.

Die vertraging moet gedeeltelik ook toegeskryf word aan die besluit om klompe entstof wat reeds in die Verenigde State aan die allerstrafste toetse, soos neergelê deur die owerheid in die Verenigde State, onderwerp is, nog verder te toets.* Voordat Amerikaanse entstof vrygestel word, word dit aan die fabrikante se eie toetse onderwerp, waarna dit nog 'n slag deur die Nasionale Stigting vir Kinderverlamming getoets word. Daarna word die entstof ook deur die Voedsel- en Geneesmiddeladministrasie

*Dit is van belang om daarop te let dat by die eerste geleentheid toe 300,000 dosisse Amerikaanse entstof deur die Unie ingevoer is, dit nie nodig geag is om die entstof aan enige biologiese toetse te onderwerp voordat dit plaaslik vrygestel is nie. Die entstof is blykbaar goedgekeur op grond van die vervaardigers se protokolle, voorgelê deur die invoerders.

ply at all times when the vaccine may be required.

The successful manufacture of poliomyelitis vaccine is inevitably fraught with difficulty and uncertainty and the South African manufacturers of the vaccine have experienced in full measure the vicissitudes which accompany mass production of this vaccine. On one occasion our local production was so far behind schedule that 300,000 doses had to be imported from the U.S.A.—a wise step which was heartily endorsed by the medical profession throughout the Union.

It is, however, disturbing to find that the distribution of the supplies of the imported vaccine, available in South Africa since the beginning of April this year, was held up for over 2 months. Partly this was due to administrative delay by the authorities in considering the situation—a most regrettable occurrence. Poliomyelitis vaccine has an expiry date which comes into effect 6 months after packaging. The tempo at which supplies of the imported vaccine must be dealt with by the licensing authority therefore needs to be accelerated considerably, particularly as any tests which it may be decided to apply will be very time-consuming. As the vaccine has a relatively short life, any Protocol or other Committee advising the Minister in these matters should be able to meet without delay, so as to deal with all batches of polio vaccine as expeditiously as possible. It is not in the best interests of a preventive programme of public health that there should be any avoidable delay in clearing batches of vaccine.

The delay has also partly been occasioned by the decision to apply tests to batches of vaccine which have already passed in the U.S.A. the most stringent tests applicable, as laid down by the United States authorities.* American vaccine, before release, passes the manufacturer's own tests and is also subjected to a repetition of testing by the National Foundation for Infantile Paralysis. Thereafter the vaccine is cleared by the Food and Drug Administration of the U.S.A., before release. Indeed, our own tests are based on the rigid specifications worked out by the American authorities and experts. In the present circumstances, the wisdom as well as the need for

* It is of interest to note that on the first occasion, when 300,000 doses of American vaccine were imported into the Union, it was not considered necessary to apply any biological tests to the vaccine before its local release. The vaccine was apparently approved on the basis of the manufacturers' protocols submitted by the importers.

van die Verenigde State goedgekeur voordat dit vrygestel word. Trouens, ons eie toetse is gegrond op die strawwe spesifikasies wat deur Amerikaanse owerhede en deskundiges uitgewerk is. In die huidige omstandighede is die verstandigheid of die noodsaaklikheid daarvan om aan te dring op die toepassing van ons eie toetse dus op verre na nie 'n uitgemaakte saak nie.

In die Verenigde Koninkryk het 'n toestand soortgelyk aan dié in Suid-Afrika ontstaan. Dit is derhalwe van belang om te lees wat die *British Medical Journal* oor hierdie saak in 'n onlangse inleidingsartikel[1] te sê het:

'Daar word gehoop dat politieke oorwegings geen rol sal speel in enige besluit om ingevoerde Salkentstof in hierlie land aan verdere toetse te onderwerp nie, maar dat sodanige toetse uitgevoer sal word aan die hand van die beste wetenskaplike raad wat op die oomblik beskikbaar is. As ons deskundiges volkome tevrede is met die toetse wat uitgevoer is met, sê nou maar, firma X se entstof in die Verenigde State, en as die toestande tydens vervoer so goed was as wat 'n mens kan verwag, kan hertoetsing van die entstof nadat dit in Brittanje aangekom het, miskien as tydverkwisting beskou word. Sonder die minste twyfel is deskundiges in die Verenigde State en Kanada net so bevoegd soos ons om doeltreffende toese uit te voer. As ons deskundiges tevrede is dat die toetse ingrypend genoeg volgens ons maatstawwe is, sal die Minister van Gesondheid dit nie moeilik vind om tot die korrekte besluit te geraak nie.'

Sonder aarseling beaam ons hierdie gesaghebbende sienswyse wat 'n duidelike leidraad tot die oplossing van dergelike probleme in ons eie land bied.

our insisting on the application of such tests is highly debatable.

In the United Kingdom a situation has arisen very similar to that which has obtained in South Africa. It is therefore of interest to read what the *British Medical Journal* stated on this very point in a recent editorial.[1]

'It is to be hoped that any decision on re-testing in this country imported Salk vaccine will not be influenced by any political considerations, but be made as a result of the best scientific advice available. If our experts are completely satisfied with tests made on, say, firm X's vaccine in the U.S.A., and conditions of transit are as good as one would expect them to be, then re-testing might be considered to be a waste of time when the vaccine arrives in Britain. There can be no doubt that experts in the U.S.A. and Canada are just as capable as we are of making efficient tests. If our experts are satisfied that the tests are stringent by our standards, then the Minister of Health will have no difficulty in coming to a correct decision.'

We have no hesitation in endorsing these authoritative views which should serve as a clear guide to the solution of similar problems in this country.

FIRST SOUTH AFRICAN MEDICO-LEGAL CONGRESS

The South African Medico-Legal Society has arranged for this Congress to be held in Johannesburg, from Thursday night, 31 July to Saturday (mid-day), 2 August 1958.

The *Patron* is the Chief Justice the Hon. Mr. H. A. Fagan. The *President* is Prof. S. F. Oosthuizen (President of the South African Medical and Dental Council). The *Vice-President* is the Hon. Mr. L. Greenberg.

The opening session at 8.15 p.m. on 31 July, will be held at Medical House, 5 Esselen Street, Hospital Hill, Johannesburg.

The sessions for the next day will be held in the new Lecture Theatre of the South African Blood Transfusion Service, corner of Klein and Esselen Streets, Hillbrow, Johannesburg.

The evening session on 1 August (to be devoted to the screening of medico-legal films) will be held in the Harveian Theatre, Medical School, Hospital Street, Johannesburg.

The following topics are scheduled for discussion:

1. *Artificial Insemination.*
2. *A Symposium on Acute Alcoholism.*
3. *Problems of Blood Transfusion.*
4. *A Symposium on Sudden Death in Infancy.*
5. *Problems of Consent to Medical Procedures.*
6. *Two Recent American Films* (in sound) entitled *The Medical Witness* and *The Doctor Defendant,* will be screened, followed by a discussion on the films, and an *Open Forum* on any topic discussed at the Congress.

These films have been sponsored by the Wm. S. Merrell Company of Cincinnati, in co-operation with the American Medical Association and the American Bar Association. They have been made specially available for this Congress by the Wm. S. Merrell Company.

7. *Medico-Legal Exhibits and a Visit to the South African Blood Transfusion Centre.*

The Congress registration fee for members of the South African Medico-Legal Society is

1. Redaksioneel (1958): *Poliomyelitis Vaccine,* Brit. Med. J., **1**, 1053 (3 Mei).

1. Editorial (1958): *Poliomyelitis Vaccine,* Brit. Med. J., **1**, 1053 (3 May).

10s. The registration fee for non-members is £1 10s. (The normal subscription for membership of the South African Medico-Legal Society is £2 2s. This includes a free subscription to the *Journal of Forensic Medicine*).

Practitioners who wish to register for attendance at this Congress must advise the Honorary Organizing Secretary not later than 15 July 1958. This will enable adequate accommodation arrangements to be made for the meetings and ensure sufficient time for the printing of a Congress prospectus which, it is hoped, will include the names and addresses of all participants in the Congress.

All communications must be directed to:

Honorary Organizing Secretary (Dr. H. A. Shapiro), First South African Medico-Legal Congress, P.O. Box 1010, Johannesburg.

SERUM LIPIDS IN THE CLINICAL PREDICTION OF CORONARY ARTERY DISEASE

AN ASSESSMENT OF THEIR VALUE

B. M. BLOOMBERG, M.D., B.CH., B.SC. (HONS.), D.T.M. & H. (RAND), D.C.P. (UNIV. LOND.)
F. LAZARUS, B.SC.
IRENE MROST, B.A.
and
RHODA SCHNEIDER, B.SC.
Clinical Laboratories, Medical Centre, Jeppe Street, Johannesburg

This paper reports studies undertaken in a series of White patients with proven or probable coronary artery disease and suitable control groups. An attempt has been made to ascertain whether an analysis of the serum total lipids, lipoprotein fractions, total cholesterol and lipoprotein cholesterol components was of clinical value in assessing the liability of an individual to develop coronary artery disease. For this reason all the lipid components were determined by methods well within the scope of a clinical laboratory. The results show that although high serum cholesterol levels are associated with coronary thrombosis, the wide ranges and overlapping of the values of all the lipid fractions in both 'normal' and diseased White groups make it hazardous, on this basis, for the clinician to predict the individual patient's liability to the disease.

MATERIAL AND METHODS

The serum lipids of 137 patients (104 males and 33 females) have been subjected to statistical analysis. Adequate clinical information, electrocardiograms, and radiological and pathological investigations were available in these cases to group them as follows:

(*a*) 'Normal', i.e. no evidence of organic disease;
(*b*) Non-vascular organic disease;
(*c*) Vascular diseases;
(*d*) Probable coronary disease, i.e. angina pectoris and a history or clinical picture suggestive of coronary thrombosis; and
(*e*) Proven coronary thrombosis, i.e. characteristic clinical and electrocardiographic findings.

Since the intention was to determine whether different lipid patterns existed while the subjects were on their customary diets, only individuals on unrestricted diets have been included in the study.

Although several of the cases of coronary thrombosis had, or were having, some form of anticoagulant treatment after the diagnosis had been established, no significant differences have been found between them and the remainder of the group, and they have not been separated in the Tables presented. The lipid values have also been analysed with reference to body weight and somatic type, but the details have not been tabulated, since again no significant differences were apparent.

Total lipids were estimated by the turbidity method of Kunkel *et al.*,[1] total cholesterol by the procedure of Pearson *et al.*,[2] and the α- and β-lipoprotein fractions and their cholesterol components by a simple modification[3] of established paper electrophoresis procedures. The β-lipoprotein fraction included both the dense β-lipoprotein band itself, and the 'trail' or 'O' fraction.[4] The analyses were done on serum separated from venous blood collected in the early morning after an overnight fast, since exercise may influence the cholesterol level after meals,[5] and comparisons of total lipids, which include the neutral fat fraction, would appear to be more valid in the fasting state. The estimations were generally done on

the day of collection, but if delayed for more than a few hours the serum was kept at 4°C. In stored specimens after 24 hours, the α-lipoprotein usually only showed a slight decrease of 1–2% with a corresponding increase in the β-lipoprotein. This is, however, within the range of experimental error, and it is authoritatively considered[6] that storage of serum at

TABLE 1: CLASSIFICATION OF SUBJECTS ACCORDING TO SERUM TOTAL LIPIDS AND TOTAL CHOLESTEROL VALUES

Group	*Total Number of Subjects*	*Age*		*Class 1. Normal Total Cholesterol: Normal Total Lipids.*		*Class 2. Normal Total Cholesterol: Raised Lipids*		*Class 3. Raised Total Cholesterol: Raised Lipids*	
		Range	*Mean*	*Number of Subjects*	%	*Number of Subjects*	%	*Number of Subjects*	%
White Males Total	**104**								
1. 'Normal'[1].	15	33–63	48	12	80.0	2	13.3	1	6.7
2. Non-vascular organic disease.	12	39–73	51	11[2]	91.7	1[3]	8.3	—	—
3. Vascular diseases excluding coronary thrombosis.	23	44–68	52	13[4]	56.5	6[5]	26.1	4[6]	17.4
4. Probable coronary disease.	19	31–67	48	11	57.9	5	26.3	3	15.8
5. Proven coronary disease.	35	33–66	50	16	45.7	11	31.4	8	22.9
White Females. Total	**33**								
6. 'Normal'[1].	4	30–63	44	3	75.0	—	—	1	25.0
7. Non-vascular organic disease.	9	30–71	49	5[7]	55.6	2[8]	22.2	2[6]	22.2
8. Vascular diseases excluding coronary thrombosis.	5	44–58	52	2[9]	40.0	3[10]	60.0	—	—
9. Probable coronary disease.	6	42–63	53	3	50.0	2	33.3	1	16.7
10. Proven coronary disease.	9	32–64	53	1	11.1	4	44.4	4	44.4
'Control'.									
11. Old Urban Bantu Males.	22	46–71	55	18	81.8	4[11]	18.2	—	—

1. No evidence of organic disease.
2. Cholelithiasis (2); ? Peptic ulcer (1); Senile osteoporosis (1); ? Addison's disease (1); Bronchitis (1); Gout (1); Chronic lymphatic leukaemia (1); Leucoderma (1); Lipomata (1); Mycosis fungoides (1).
3. Duodenal ulcer (1).
4. Hypertension (3); Peripheral vascular disease (4); Diabetes mellitus (2); Bundle branch block (2); Aortic stenosis (1); Retinal vein thrombosis (1).
5. Hypertension (2); Peripheral vascular disease (4).
6. *See* Table 2.
7. Adrenogenital syndrome (1); Gaucher's disease (1); Cholelithiasis (1); Disseminated sclerosis (1); Senile osteoporosis (1).
8. Adrenogenital syndrome (1); Senile osteoporosis (1).
9. Hypertension (1); Peripheral vascular disease (1).
10. Aneurysmal dilatation of descending aorta (1); Auricular fibrillation (2).
11. One case of diabetes mellitus, and 1 case of vascular disease.

0–5°C. for periods up to 28 days produces no alteration of the lipoprotein pattern or content.

In view of the difficulty of assessing the normality of the 'normal' group of White males, the White groups have also been compared with a 'control' group of 20 apparently healthy urban Bantu males of similar ages and in better economic circumstances than the average Bantu. This group would appear to provide a more suitable 'normal', since thrombotic complications of atherosclerosis are rare in the Bantu[7] and severe atherosclerosis itself uncommon.[8] Lipid patterns of the Bantu have already been shown to differ significantly from those of White South Africans,[9-15] although there is some difference of opinion regarding the actual incidence of milder degrees of atherosclerosis in these peoples.[7, 8, 16]

RESULTS

In Table 1 the subjects have been classified according to the serum total lipid and total cholesterol values.

Class 1 includes all the subjects whose total lipids were below 700 mg. per 100 ml. and whose cholesterol concentrations were below Keys'[17] upper limit for 90% of an American population of the same ages. These upper limits ranged from 219 mg. per 100 ml. at 18 years to a maximum of 332 mg. per 100 ml. at 55 years, and thereafter a gradual decrease to 276 mg. per 100 ml. at 75 years of age. Cholesterol levels reported for South African Whites[9, 10] and our own unpublished figures are of the same order.

Class 2 includes all subjects whose total lipids were above 700 mg. per 100 ml. but whose cholesterols were below the same upper limits as Class 1.

Class 3 includes all subjects showing total lipids above 700 mg. per 100 ml. and total cholesterols *above* Keys' upper limits.

It will be seen that the percentage distribution in Classes 2 and 3 increases in the White male subjects with vascular disease, probable coronary disease, and proved coronary thrombosis. Although the number of White female subjects is small, the number of cases in Classes 2 and 3 is proportionally greater than among the White males. In particular the high percentage of cases of coronary thrombosis with

TABLE 2[1]: SERUM LIPID VALUES IN 24 WHITE SUBJECTS WITH RAISED TOTAL CHOLESTEROL AND RAISED TOTAL LIPIDS (CLASS 3)

Group[2]	*Number of Subjects*	*Total Cholesterol Mg. per 100 ml.*	*α-Cholesterol*		*β-Cholesterol*		*Total Lipids*	*α-Lipoprotein*	*β-Lipoprotein*
			Mg. per 100 ml.	*% Total*	*Mg. per 100 ml.*	*% Total*	*Mg. per 100 ml.*	%	%
Males	**16**								
1.	1	309	43	14	266	86	730	11	89
3.	4[3]	338–365 (351)	30–45 (36)	9–13 (10)	308–325 (315)	87–91 (90)	830–1377 (1027)	10–18 (15)	82–90 (85)
4.	3	298–363 (336)	17–47 (32)	5–13 (10)	263–331 (304)	87–95 (90)	768–1000 (855)	5–27 (16)	73–95 (84)
5.	8	280–381 (340)	4–51 (37)	1–14 (11)	241–377 (303)	86–99 (89)	710–1562 (985)	6–18 (13)	82–94 (87)
Females	**8**								
6.	1	356	50	14	306	86	900	11	89
7.	2[4]	320–388 (354)	35–58 (47)	9–18 (14)	262–353 (307)	82–91 (86)	880–910 (895)	11–24 (18)	76–89 (82)
9.	1	355	53	15	302	85	1040	38	62
10.	4	280–424 (345)	34–58 (47)	8–17 (14)	234–390 (298)	83–92 (86)	770–1007 (891)	16–22 (18)	78–84 (82)

1. Since the number of subjects in each group is small, the data have not been subjected to statistical analysis. *Range* and the *Mean* (bracketed) only are recorded.
2. Groups as in Table 1.
3. Hypertensive heart disease (1); Diabetes mellitus (1); Cerebral atherosclerosis with Parkinson's disease (1); Atherosclerosis with macular degeneration (1).
4. Obesity and cholelithiasis, developed coronary thrombosis 18 months later (1); osteoporosis of spine (1).

raised lipids and raised total cholesterols (Class 3) is noteworthy.

In Table 2 the ranges and mean values for the various lipid fractions of all Class 3 cases are summarized. Of 16 males, evidence of vascular disease was found in 15; and of 8 females, 4 had proven coronary thrombosis. Of the 2 cases of non-vascular organic disease, one suffered an attack of coronary thrombosis 18 months after the blood lipids were studied. Hypercholesteraemia and hyperlipaemia are, therefore, commonly associated with coronary thrombosis and although the aetiological relationship is not clear, the hazard of thrombosis may with good reason be feared in such individuals.

In order to determine whether differences exist in normocholesteraemic subjects, a statistical analysis of the data in Classes 1 and 2 was carried out, and the more important conclusions follow. The wide ranges for the various lipid components and the large standard deviations are noteworthy. For these reasons statistically significant differences have been assessed above the 99% probability level (i.e. $P<0.01$).

TOTAL CHOLESTEROL AND LIPOPROTEIN CHOLESTEROL FRACTIONS (TABLE 3)

The mean total cholesterol value of the coronary thrombosis group of White males (Group 5) shows only a possibly significant increase ($P = 0.02$) when compared to 'normal' White males (Group 1), whereas the small coronary thrombosis group of White females (Group 10) shows a more significant increase ($P<0.01$). All the abnormal White groups, however, have higher mean total cholesterol levels than have the members of the normal group.

A comparison of the cholesterol fractions of the abnormal White male groups with the 'normal' White males (Group 1) shows similar α-cholesterol percentages and concen-

TABLE 3[1] SERUM TOTAL CHOLESTEROL AND LIPOPROTEIN CHOLESTEROL FRACTIONS IN NORMOCHOLESTERAEMIC SUBJECTS (CLASSES 1 AND 2)

Group[2]											
	Number of Subjects	*Total Cholesterol*		*α–Lipoprotein Cholesterol*				*β–Lipoprotein Cholesterol*			
		Mg. per 100 ml.		*Mg. per 100 ml.*		*% Total*		*Mg. per 100 ml.*		*% Total*	
		Range	*Mean ± SD.*	*Range*	*Mean ± SD.*	*Range*	*Mean ± SD.*	*Range*	*Mean ± SD.*	*Range*	*Mean ± SD.*
White Males.											
1.	14	169–259	221±26	14– 49	35±10	8–21	16± 4	149–214	186±21	79–92	84± 4
2.	12	175–289	218±36	25– 58	36±11	9–26	17± 5	137–263	182±38	74–91	83± 5
3.	19	132–305	233±46	15– 48	36±10	7–30	16± 5	92–274	197±43	70–93	84± 5
4.	16	184–295	231±37	20– 58	38±12	9–24	17± 5	156–260	193±37	76–91	83± 5
5.	27	164–332	246±40	14– 69	36±13	5–27	15± 5	139–276	210±39	73–95	85± 5
White Females.											
6.	3[3]	165–268	223±37	30– 70	45±16	8–34	21± 8	109–236	178±41	66–92	79± 8
7.	7										
8.	5	214–310	257±38	30– 63	46±12	11–24	18± 6	163–263	211±41	76–89	82± 6
9.	5	204–288	249±32	32–117	65±36	14–47	26±14	131–239	183±41	53–86	74±14
10.	5	236–321	277±34	19– 72	41±20	8–25	15± 6	217–273	236±27	75–92	85± 6
'Control'.											
11.	20[4]	165–270	215±28	21–115	70±24	9–62	33±12	63–216	145±37	38–91	67±12

1. The detailed statistical analysis has been omitted.
2. Groups as in Table 1.
3. As the number of 'normal' females is small, Groups 6 and 7 have been combined.
4. The cases of diabetes mellitus and 'vascular disease' have been omitted.

trations throughout. Although β-cholesterol percentages show no significant differences, the actual β-cholesterol concentrations are higher in the abnormal groups and the increase becomes of possible significance (P = 0.02) in the coronary thrombosis group (Group 5). It should, however, be noted that the β-cholesterol concentrations of the female coronary thrombosis group (Group 10) is considerably higher (P<0.01) while the concentration of α-cholesterol is lower and approaches that of Group 1 and the other White male groups. The decrease in the α-fraction combined with the increase in the β-fraction may be of fundamental importance and is further considered in the section on *Discussion*.

It is of interest in view of previous reports[9] that normal Whites and Bantu of comparable age groups show similar ranges and mean total cholesterol values. The higher total cholesterol levels found for the Bantu group in this study may be related to their higher income level and standard of living,[15] compared to the average Bantu. Despite this lack of difference of the total cholesterol values, a comparison of the lipoprotein cholesterol fractions of the normal Whites and Bantu, however, shows that the former has significantly lower (P<0.01) α-lipoprotein cholesterols and significantly higher (P<0.01) β-lipoprotein cholesterols. This difference holds for the abnormal White male and female groups (except Group 9). However, it is apparent that the actual α-cholesterol concentrations of these White female groups are higher than those of the White male groups and approach those of the Bantu (Group 11). These differences are of considerable importance and will be reported more fully elsewhere,[15] but it may be noted here that the lipoprotein pattern of the Bantu approaches that of young White females, which may be significant since the Bantu have higher oestrogen : androgen ratios than have Whites.[18]

TABLE 4[1]: SERUM TOTAL LIPIDS AND LIPOPROTEIN FRACTIONS IN NORMOCHOLESTERAEMIC SUBJECTS (CLASSES 1 AND 2)

Group[2]	*Number of Subjects*	*Total Lipids*		*α-Lipoprotein*		*β-Lipoprotein*	
		Mg. per 100 ml.		*% Total Lipids*		*% Total Lipids*	
		Range	*Mean ± SD.*	*Range*	*Mean ± SD.*	*Range*	*Mean ± SD.*
White Males.							
1.	14	470–980	584±61	7–30	19±8	70–93	81±8
2.	12	473–820	612±90	6–26	18±7	74–94	82±7
3.	19	470–960	663±135	7–34	19±8	66–93	81±8
4.	16	449–965	643±144	6–48	20±11	52–94	80±11
5.	27	463–850	657±112	7–31	17±6	69–93	83±6
White Females.							
6.	3[3]	495–790	635±87	14–40	27±9	60–86	73±9
7.	7						
8.	5	503–1000	733±196	10–39	23±10	61–90	77±10
9.	5	666–759	707±39	14–36	24±8	64–86	76±8
10.	5	599–882	781±114	14–23	18±4	77–86	82±4
'Control'.							
11.	20[4]	490–760	617±75	0–52	26±14	48–100	74±14

1.
2.
3.
4.
See Footnotes Table 3.

TOTAL LIPIDS AND LIPOPROTEIN FRACTIONS (TABLE 4)

No significant differences have been found between the total lipids of 'normal' and abnormal White male groups, although the mean levels are higher in the latter. The abnormal female groups (8–10), however, show significant increases ($P<0.01$) compared to the 'normal' White males. It is noteworthy that the probable and proven coronary disease groups and the other (vascular) diseases group of White females, though small, show relatively gross increases in total lipids. Attention has already been directed to the higher proportion of Class 3 cases among the female subjects, so that coronary thrombosis in White females appears to be more obviously associated with abnormally raised lipids than it does in males. The abnormal White groups show similar differences when compared to the 'control' Bantu group, but the latter shows no significant difference from the 'normal' White males ($P = 0.2$).

Statistical comparisons of the percentages of the two lipoprotein fractions in the different groups requires caution in view of the wide ranges of values. However, the closeness of the means of all the White male groups is noteworthy, as is also the fact that these means differ considerably from those of the 'control' Bantu, although not statistically significant at the 99% level. The lipoprotein patterns of the different groups of White females follow the cholesterol fractional pattern and again are closer to the Bantu than to the White males, except in the coronary thrombosis group where the decrease in the α-lipoprotein and the increase in the β-lipoprotein are again marked.

DISCUSSION

In countries where myocardial infarction is 'endemic', normality does not necessarily mean freedom from atherosclerosis.[19] Since the South African White population shows a high incidence of atherosclerosis, whereas the South African Bantu is not severely afflicted,[8] it must be accepted that the White subjects in this study who showed no evidence of organic disease were unlikely to be free from atherosclerosis. The differences between the α- and β-lipoproteins and their cholesterol components of the 'normal' groups of Whites and Bantu, despite the similarity of their total cholesterol values are, therefore, of considerable significance. These results are supported by the finding[13] that the S_f 12–20 and S_f 20–100 classes of β-lipoprotein of the South African Bantu are markedly lower than the 'normal' levels for a sample of the New York City White population.

Examination of our data shows that the crux of the problem of demonstrating an association between serum lipids and atherogenesis, is the difficulty of assessing the 'normality' of control groups. While our normocholesteraemic cases of coronary thrombosis show highly significant differences compared to the Bantu, marked differences have not been found between our 'normal' White subjects and cases of proved coronary thrombosis. This has led us to conclude that so-called 'normal' subjects and normocholesteraemic patients with coronary artery disease cannot be reliably differentiated by their lipoprotein patterns. Our results on normal Bantu[15] have led us to suggest that ideal values of α-lipoprotein cholesterol are 60–70 mg. per 100 ml. and for β-lipoprotein cholesterol 110–120 mg. per 100 ml., and further that a decrease in the α-level combined with an increase in the β-level favours the development of atherosclerosis. Judged by these criteria, all the normocholesteraemic White subjects in this study may be considered abnormal.

Other authors[20] have, however, concluded that normocholesteraemic patients with proven coronary artery disease did show alterations in lipoprotein pattern similar to those obtained in patients with hypercholesteraemia, α-lipoprotein percentages being depressed and β-lipoprotein increased compared to normal controls. The basis of the apparent disagreement between our results and those of Bossak *et al.*[20] lies in the 'normal' values of their control groups, the composition of which is not stated. Since these values are similar to our 'normal' Bantu group, and quite different from our 'normal' Whites, no true comparison of the findings is possible.

While the material presented here was being analysed, a comprehensive co-operative study on lipoproteins and atherosclerosis in the United States of America was published.[6] All the participants in this co-operative study agreed in finding that although atherosclerosis, as manifested by clinical signs of coronary artery disease, was associated with a disorder of lipid metabolism, serum total cholesterol values were not of clinical use in predicting which individuals would develop coronary heart disease. In a more recent report,[21] the Harvard group have detailed their findings on large groups of apparently healthy adults and

those with coronary heart disease. They concluded that

'the large variability of serum lipid levels in adults of similar age and sex and clinical status, and the small differences between apparently well people and those with angina pectoris or myocardial infarction prevented efficient application of serum cholesterol and lipoprotein levels by themselves to the clinical prediction of coronary heart disease among individuals.'

Despite the evidence, therefore, of an association between the levels of the various serum lipid fractions and the incidence of coronary artery disease, and the fact that the differences between the various groups are present to a greater or lesser degree in all the lipid components estimated in this study, it is apparent that it is not feasible to assess a particular individual's liability to coronary artery disease when the total cholesterol is within the limits at present considered 'normal.' When the serum cholesterol is raised beyond these limits, the results tend to show an increased risk of developing coronary thrombosis, but again it is hazardous for the clinician to 'predict' the individual outcome. This conclusion, which has been reached by the majority of investigators, can only mean that the disturbance of the lipid transport system which predisposes to and appears to be an essential condition for myocardial infarction[19] is not the immediate cause of the infarction. Thus while the aetiological relationship between lipid transport and atherosclerosis remains uncertain, the problem is further complicated by using the term atherosclerosis to include

'anything from experimental fatty lesions in the aorta of rabbits to the whole of the natural history of ischaemic heart disease in man. This widespread contemporary woolliness has had unfortunate results.'[22]

Nevertheless, the considerable degree of correlation emphasizes the necessity for further studies of the differences in other serum lipid components in communities with varying incidences of atherosclerosis.

SUMMARY

An attempt has been made to ascertain whether an analysis of the serum total lipids, lipoprotein fractions, total cholesterol and lipoprotein cholesterol components was of clinical value in assessing the liability of an individual to develop coronary artery disease. For this reason all the lipid components were determined by methods well within the scope of a clinical laboratory.

The results obtained in the various groups of subjects have been divided into 3 classes:

(1) Total cholesterol and total lipids within or below 'normal' range;
(2) Normal cholesterol and raised total lipids;
(3) Raised cholesterol and raised total lipids.

While the 'normal' White males, and the White males with non-vascular diseases, show a similar class distribution, the percentage distribution in Classes 2 and 3 increases in the male subjects with vascular diseases, probable coronary disease, and proved coronary thrombosis. Although the number of White female subjects is small, the number of cases in Classes 2 and 3 is proportionally greater than among the White males. In particular, the high percentage of cases of coronary thrombosis with raised lipids and raised total cholesterols (Class 3) is noteworthy. It is, therefore, obvious that hypercholesteraemia and hyperlipaemia are commonly associated with coronary thrombosis and, from the clinician's viewpoint, may be considered to increase the hazard particularly in female subjects.

A statistical analysis of subjects in Classes 1 and 2 is presented. The experimental results show a wide range of values for the various lipid components within all the groups studied and there are also considerable deviations from the mean values. Although the higher serum cholesterol levels among Whites are associated with coronary thrombosis, the wide ranges and overlapping of the results preclude the assessment of the individual patient's liability to the disease from the level of his serum total cholesterol. However, the proven coronary thrombosis group of White males does show a doubtful increase when compared to 'normal' White males, and the coronary thrombosis group of White females shows a highly significant increase.

When compared with the urban Bantu group, all the normocholesteraemic White subjects in this study may be considered abnormal. This conclusion is supported by the high incidence of atherosclerosis, despite apparent good health, of the South African White population. These findings emphasize that the clinician is unlikely to be assisted by the serum lipids in his problem of anticipating attacks of coronary thrombosis and of determining individual susceptibility when the serum cholesterol is not grossly abnormal.

OPSOMMING

'n Poging is aangewend om uit te vind of 'n ontleding van die serum-totaal-lipiede, lipoproteïenfraksies, totale cholesterol en lipoproteïen-cholesterolbestanddele van enige kliniese waarde is by die vas-

stelling van 'n persoon se vatbaarheid vir koronêre slagaarkwaal. Om hierdie rede is al die lipiedbestanddele vasgestel met behulp van metodes wat maklik binne die bestek van 'n kliniese laboratorium is.

Die resultate wat met verskillende groepe persone behaal is, is in 3 klasse verdeel:

1. Totale cholesterol en totale lipiede binne of benede die ‚normale' bestek;
2. Normale cholesterol en vermeerderde totale lipiede;
3. Vermeerderde cholesterol en vermeerderde totale lipiede.

Terwyl ‚normale' blanke mans en blanke mans met nie-vaskulêre kwale 'n ooreenstemmende klasdistribusie openbaar, vermeerder die persentasiedistribusie in Klasse 2 en 3 by mans met vaatkwale, verdagte koronêre kwale, en bewese koronêre trombose. Hoewel die aantal blanke vroue klein is, is die aantal gevalle in Klasse 2 en 3 na verhouding groter as onder blanke mans. Veral opvallend is die hoë persentasie van gevalle van koronêre trombose met vermeerderde lipiede en vermeerderde totaal-cholesterols (Klas 3). Dit is derhalwe duidelik dat hipercholesteremie en hiperlipemie gewoonlik geassosieer is met koronêre trombose. Uit die oogpunt van die klinis kan daar ook uitgegaan word van die standpunt dat dit die gevaar verhoog—veral by die vrou.

'n Statistiese ontleding van die persone in Klasse 1 en 2 word aangebied. Die proefondervindelike resultate openbaar 'n groot verskeidenheid van waardes vir die verskillende lipiedbestanddele binne al die groepe wat bestudeer is, en daar was ook aansienlike afwykinge van die gemiddelde waardes. Hoewel die hoër serum-cholesterol-peile onder blankes met koronêre trombose geassosieer is, maak die groot afwykinge en oorvleueling dit onmoontlik om die individuele pasiënte se vatbaarheid vir die siekte vas te stel aan die hand van die peil van die serum-totaal-cholesterol. Hoe dit ook al sy, die groep blanke mans met bewese koronêre trombose openbaar 'n twyfelagtige vermeerdering as hulle met ‚normale' blanke mans vergelyk word, en die groep blanke vroue met koronêre trombose toon 'n hoogs betekenisvolle vermeerdering.

In vergelyking met die stedelike Bantoe-groep kan al die normaal-cholesteremie-blankes wat bestudeer is, as abnormaal beskou word. Hierdie gevolgtrekking word gestaaf deur die hoë voorkoms van aterosklerose, ondanks oënskynlike goeie gesondheid, onder die blanke bevolking van Suid-Afrika. Hierdie bevindings beklemtoon dat die klinis waarskynlik geen hulp van die serum-lipiede sal kry by die oplossing van die probleem waarvoor hy te staan kom nie, nl. om aanvalle van koronêre trombose te antisipeer en om die individu se vatbaarheid vas te stel wanneer die serum-cholesterol nie uitermate abnormaal is nie.

Our thanks are due to our many clinical colleagues in Johannesburg for allowing us access to cases under their care, and for their unfailing courtesy and co-operation during the course of this study.

REFERENCES

1. Kunkel, H. G., Ahrens, E. H. and Eisenmenger, W. J. (1948): *Application of Turbidimetric Methods for Estimation of Gamma Globulin and Total Lipid to the Study of Patients with Liver Disease.* Gastroenterol., **11,** 499.
2. Pearson, S., Stern, S. and McGavack, T. H. (1952): *A Rapid Procedure for the Determination of Serum Cholesterol.* J. Clin. Endocrinol. Metab., **12,** 1245.
3. Bloomberg, B. M., Jankelowitz, R. and Lazarus, F. (1955): *A Simple Paper Electrophoresis Procedure for the Determination of the Percentage Concentration of Serum α- and β-Lipoproteins and their Cholesterol Components.* S. Afr. J. Med. Sci., **20,** 140.
4. Adlersberg, D., Bossak, E. T., Sher, I. H. and Sobotka, H. (1955): *Electrophoresis and Monomolecular Layer Studies with Serum Lipoproteins.* Clin. Chem., **1,** 18.
5. Keys, A., Anderson, J. T. and Michelsen, O. (1956): *Serum Cholesterol in Men in Basal and Nonbasal States.* Science, **123,** 2.
6. *Report of the Technical Group and Committee on Lipoproteins and Atherosclerosis of the National Advisory Heart Council* (1956): *Evaluation of Serum Lipoprotein and Cholesterol Measurements as Predictors of Clinical Complications of Atherosclerosis: Report of a Cooperative Study of Lipoproteins and Atherosclerosis.* Circulation, **14,** 691.
7. Becker, B. J. P. (1946): *Cardio-Vascular Disease in the Bantu and Coloured Races of South Africa*: IV. Atheromatosis. S. Afr. J. Med. Sci., **11,** 97.
8. Higginson, J. and Pepler, W. J. (1954): *Fat Intake, Serum Cholesterol Concentration, and Atherosclerosis in the South African Bantu. Part II*: *Atherosclerosis and Coronary Artery Disease.* J. Clin. Invest., **33,** 1366.
9. Walker, A. R. P. and Arvidsson, U. B. (1954): *Fat Intake, Serum Cholesterol Concentration, and Atherosclerosis in the South African Bantu. Part I*: *Low Fat Intake and the Age Trend of Serum Cholesterol Concentration in the South African Bantu.* J. Clin. Invest., **33,** 1358.
10. Bronte-Stewart, B., Keys, A., Brock, J. F., Moodie, A. D., Keys, M. H. and Antonis, A. (1955): *Serum Cholesterol, Diet and Coronary Heart Disease.* Lancet, **2,** 1103.
11. Bersohn, I. and Wayburne, S. (1956): *Serum Cholesterol Concentration in New-Born African and European Infants and their Mothers.* Amer. J. Clin. Nutr., **4,** 117.
12. Bloomberg, B. M. (1956): *Serum Lipoproteins in Relation to Atherosclerosis and Coronary Thrombosis* (1956): S. Afr. Practit., **1,** 253, 349, 429, 478
13. Ruskin, H. D., Cohn, T. D., Greenblatt, I. J. and Bloomberg, B. M. (1956): *Serum Beta-Lipoprotein Studies in the South African Bantu.* Circulation, **14,** 992.
14. Walker, A. R. P. and Bersohn, I. (1957): *Why Atherosclerosis?* in *Medicine in South Africa.* Supplement to S. Afr. Med. J., pp. 106–114.
15. Bloomberg, B. M., Lazarus, F., Mrost, I. and Schneider, R. *Serum Lipids in South African Bantu and White subjects.* To be published. (Circulation).
16. Woods, J. D. and Laurie, W. (1957): *Atherosclerosis in the Bantu.* Lancet, **1,** 1091.
17. Keys, A., Mickelsen, O., Miller, E. v. O., Hayes, E. R. and Todd, R. L. (1950): *The Concentration of Cholesterol in the Blood Serum of Normal Man and its Relation to Age.* J. Clin. Invest., **29,** 1347.
18. Bloomberg, B. M., Miller, K., Keeley, K. J. and Higginson, J. Urinary Oestrogens and Neutral

17-Ketosteroids in the South African Bantu with and without Hepatic Disease. (*To be published*).
19. Leading Article (1957): *Serum Cholesterol and Myocardial Infarction.* Lancet, **1**, 1286.
20. Bossak, E. T., Wang Chun, I. and Adlersberg, D. (1956): *Studies of Serum Proteins, Lipids and Lipoproteins in Coronary Atherosclerosis in Man.* Circulation, **14**, 914.
21. Lawry, E. Y., Mann, C. V., Peterson, A., Wysocki, A. P., O'Connell, R. and Stare, F. J. (1957): *Cholesterol and Beta-Lipoproteins in the Serums of Americans: Well Persons and those with Coronary Heart Disease.* Amer. J. Med., **22**, 605.
22. Morris, J. N. (1956): *Fats and Disease.* (Letter to the Editor). Lancet, **1**, 687.

THE RELIEF OF PAIN WITH MORPHINE AND AMIPHENAZOLE

R. A. FLEMING, *O.B.E.* (MIL.), M.B., M.S., F.R.C.S., F.I.C.S.
Baragwanath Hospital, Johannesburg

Opium derivatives, especially morphine, have been used for countless years to relieve pain and its associated mental problems. Unfortunately, adequate doses may be accompanied by undesirable side effects, particularly dangerous depression of respiration, narcosis, and stimulation of the vomiting centre. These complications force clinicians to administer small doses frequently, but this results in only partial analgesia. During World War II, larger amounts were given to the fit, young servicemen with good effects and few problems, but this is not easily translated into civilian practice.

In recent years pethidine has been used almost exclusively for pain relief, but this, other than for relief of muscle spasm, is short-lived, incomplete and relatively unsatisfactory —particularly from the sufferer's point of view. Perhaps pethidine is popular because it is believed to be safer than the morphine derivatives; but if the dosage is increased to give the same degree of analgesia as morphine, the side effects, including addiction, become just as severe. Holmes' clinical evaluation of the drugs in obstetric practice suggests that pethidine 150 mg. is equivalent to morphine gr. ¼ (16 mg.).[1]

If pain is completely relieved and a reasonable period of analgesia ensues, the sufferer immediately adopts a mentally tranquil attitude—'should the pain return, the doctor can obviously relieve it completely again.' This gives him a stoicism to the mild discomfort which may accompany subsequent natural healing. Conversely, incomplete relief of pain leads to psychosomatic problems: the pain threshold is lowered by an acute anxiety produced by fear of greater unknown pain to come, and a worry that the doctor cannot, or will not, banish the suffering. This problem is often seen in treating patients with chronic pain.

In this investigation, Daptazole brand of amiphenazole was used in combination with large doses of morphine to achieve complete analgesia. Amiphenazole has a remarkable and lasting antagonism to the effects on the vomiting centre and on respiratory and narcotic depression, but it has an insignificant effect on the analgesic action of morphine. This drug combination was also used as the sole analgesic agent during many minor and a few major operations. This latter conception is merely a modern revival of morphine usage in the pre-anaesthesia era.

CHEMISTRY OF AMIPHENAZOLE

Amiphenazole is 2:4-diamino-5-phenylthiazole hydrochloride. The injection is prepared by the addition of 2 c.c. of physiological saline to 30 mg. amiphenazole. As it is compatible with morphine, a solution of morphine instead of saline may be used to dissolve the amiphenazole. The resulting colourless solutions are stable at room temperature for up to 24 hours, and may be stored in a refrigerator for 7 days.

PHARMACOLOGY

The actions of amiphenazole as a morphine antagonist in Man may be summarized as follows:

i. Morphine-induced respiratory depression is counteracted.

ii. Vomiting and constipation due to morphine are lessened.

iii. Morphine depression of the cough reflex is counteracted.

iv. McKeogh and Shaw[4] commented on the bright mental outlook in their cases of hopeless malignancy with pain when this drug combination was given—it lessened when the amiphenazole was withdrawn. Neither tolerance or addiction was seen in over 150 cases in which large doses of morphine with amiphenazole were administered for many months.

Amiphenazole may be given intravenously, intramuscularly, subcutaneously or by mouth. With morphine, the usual doses are: intravenously or intramuscularly 20–30 mg.; orally 20–60 mg.

SIDE EFFECTS AND PRECAUTIONS

Amiphenazole in therapeutic doses in patients having morphine causes few, if any, side effects. Occasionally slight irregular twitchings of the

fingers, neck and shoulders are noticed, but these cannot be differentiated from exactly similar movements seen in deeply morphinized patients without amiphenazole.

The morphine-amiphenazole combination is very safe, but the respiration and the degree of sedation must be watched. Slow and irregular breathing is not a sign of respiratory danger, provided the respirations are deep and there is no cyanosis. Under these conditions even a respiratory rate as low as 6 per minute is not dangerous. If respirations fall below 6 per minute, becoming shallow or accompanied by cyanosis, further amiphenazole can be given. This will result in increased depth rather than frequency of respiration, and cyanosis will disappear.

In this investigation, an unrecorded side effect of generalized sweating was seen, usually in patients where pain relief was incomplete.

The morphine-amiphenazole combination was used on 389 cases in the principal ward at a very large non-European hospital.* The patients treated were Zulu, Bantu, Xosa and Coloured. The drug combination was used as:

1. A post-traumatic analgesic agent.
2. A post-operative analgesic agent.
3. The sole analgesic agent during 196 minor operations.
4. The sole analgesic agent during 5 major operations.

To minimize the variables and to obtain accurate information, the following base line specifications were rigidly observed:

(*a*) A standard 'unit' of morphine gr. ½ (32 mg.) and amiphenazole 25 mg. (the quantity which can be withdrawn from a vial containing 30 mg.) was used.

(*b*) This unit was always given intramuscularly.

(*c*) A standard form was drawn up for recording all the necessary observations (Fig. 1).

(*d*) This form was planned to make the recordings mainly observations of time intervals, this being the simplest measurement for young interns and African nursing staff to make.

(*e*) Assessment of pain relief had 3 separate checks, the patient, the nurse and the attending doctor all giving evidence on this quite unmeasurable entity. It was felt that, should the standard unit dose be too small, it would have to be repeated sooner and its inefficiency would be reflected in the time interval between injections. The degree of maximum relief was also noted.

(*f*) The chief side effects mentioned specifically on the form were vomiting, muscle twitching, cyanosis, constipation, delirium and the state of consciousness. The temperature, pulse and respiration were also examined for undue irregularities. An unreported side effect of generalized sweating was noted early in the series, and this feature was subsequently noted on the form.

* Baragwanath Hospital, Johannesburg.

CLINICAL OBSERVATIONS ON THE USE OF MORPHINE AND AMIPHENAZOLE IN MISCELLANEOUS SURGICAL CONDITIONS

The trial itself was divided into 2 phases: a preliminary trial on 40 patients (to give the medical and nursing staff experience in handling and using the combination and recording observations) and the main trial (on 349 patients).

Certain points of interest emerged from the preliminary trial:

(*a*) There was relief of pain with the morphine-amiphenazole injection in from 10–30 minutes; 86% of cases obtained 100% relief of pain; 7% obtained 80% relief and 3% obtained 60%. The remaining 4% only obtained 50% relief. Many patients required one standard dose only. The average duration of sustained analgesia was 9 hours, as judged by the intervals between the administration of first and second standard units. In multiple dosage the duration of analgesia progressively increased.

(*b*) The relative duration of action of morphine and of amiphenazole was found to be different. For about 4½–5½ hours the patients on the combination were alert, awake and responsive. After this, some became drowsy and tended to doze, indicating that the effect of the amiphenazole had worn off.

(*c*) With morphine-amiphenazole, the effect of subsequent relaxants was intensified or their neutralization was made more difficult.

Case 1 illustrates this ? potentiation of morphine-amiphenazole.

Case 1: A patient with an internal strangulation of the ileum, a direct sequel of a hysterectomy performed 2 years before, was given 1 unit of morphine-amiphenazole (as premedication) and Pentothal, nitrous oxide and oxygen with a curare relaxant for resection of about 2 feet of ileum.

The operation took 35 minutes and, apart from slight cyanosis during Pentothal induction, all was well until the last few skin sutures, when she collapsed and became deeply cyanotic. Spontaneous respiration did not recur, despite continued intubation, oxygenation and antidotes to the relaxant. This was a true respiratory failure death.

Accordingly, in subsequent cases relaxants were either omitted or administered in only 50% of the usual dosage. With this procedure no further problems occurred.

(*d*) Amiphenazole had the ability to counteract morphine-induced respiratory depression (Case 2).

Case 2: A male of 55 years was suffering from a pneumo-haemo-thorax following stab wounds of the chest. He was ordered 1 standard unit of morphine and amiphenazole for pain. Owing to an oversight, a relieving staff nurse gave the morphine only. The patient was later (? interval) discovered to be deeply unconscious, with sporadic, shallow and ineffective

respirations, marked cyanosis and pin-point pupils; 30 mg. amiphenazole were given intravenously forthwith, whilst a B.L.B. mask and oxygen were being brought. Within 40 seconds the respirations had deepened, become rhythmic and were slowly increasing in frequency, the cyanosis abating. Within 3 minutes the patient was conscious enough to speak intelligently to the doctor, and the pupils returned to normal about the same time.

The information which follows combines the cases treated during the preliminary and the main trial.

For convenience, the cases have been grouped into 9 main headings, according to the surgical procedure necessary.

Thoracic Injuries: (75 *Patients aged* 10–70+ *Years*). There were 53 multiple

BARAGWANATH HOSPITAL

Name ..... *Age* ..... *Occupation* ..... *Hospital No.* .....

Final Diagnosis:

Result: Cured ☐ Improved ☐ Unchanged ☐ Death ☐

Time and Date of Admission: ..... *Date of Discharge* .....

Accident ☐ Routine Admission ☐

Pain:

(*a*) Patient's description: *Very Severe* ☐ *Severe* ☐ *Mild* ☐ *Nil* ☐

(*b*) Doctor's description: *Very Severe* ☐ *Severe* ☐ *Mild* ☐ *Nil* ☐

Shock: Doctor's description: *Very Severe* ☐ *Severe* ☐ *Mild* ☐ *Nil* ☐

Operation: (Nature, Date, Time of Start and Finish).

Anaesthesia: (All Agents Used. Time of Start and Finish).

Times: Patient conscious .....

Patient complains of post-operative pain .....

INJECTIONS OF MORPHINE AND DAPTAZOLE

STANDARD DOSAGE UNITS MORPHINE ½ GR. (32 MG. DAPTAZOLE (25 MG.)

Amounts in mg.		*Time and Date of Injection Given*	*Time and Date of Onset of Relief*	*Degree of Relief*	*Time Renewal of Pain*	*Vomiting*	*Muscle Twitching*	*Cyanosis of Mucosa*
M.	*D.*							

1. Summary of Patient's Respiration, Pulse and Temperature Charts.
2. Summary of Untoward Complications.
   Chest:
   Constipation:
   Delirium:
   Others:
3. Summary of:
   Amount of Morphine Used
   Amount of Daptazole Used
   Number of Injections
   Intervals between Injections
4. Summary of Patient's Description of his Experiences.
5. Summary of Doctor's Observations Regarding Relief of Pain, etc.

Fig. 1. Standard form used for recording observations.

penetrating wounds of the thorax, 12 fractures of the thoracic cage and 10 single penetrating wounds of the thorax.

Over half the cases had a gross pneumothorax and 45 were severely cyanosed. In all patients the rate of respiration was between 15 to 40+ per minute.

After the first injection of morphine-amiphenazole, all but 6 patients experienced pain relief ranging from 60% to 100%. In half the cases the pain was completely relieved. Those with minimal pain relief still experienced 50% alleviation of pain.

The clinical notes comment on marked decrease in frequency and increase in depth of respiration.

In 4 patients thoracic rehabilitation was commenced in as short a period as 2 hours and after 6 hours 48 patients were doing breathing exercises.

Apart from 11 cases who experienced generalized sweating (all these patients experienced a lesser degree of pain relief) there were no other side effects of therapy.

Of the 75 patients 65 had an uninterrupted and complete recovery from the surgical procedure.

All patients commented on the great improvement in ability to breathe freely after the pain was relieved—even the cases who later required relief of tension pneumothorax, though this improvement was increased by this latter procedure. The medical staff confirmed this improvement.

Many of these cases were admitted with a large degree of pain, rapid, shallow breathing and cyanosis. In our considerable experience of the morbid results of this type of trauma (stabbing is the commonest method of assault in this Province) it has been noticed that patients with pneumothoraces and minimum lung damage do not cough much, but when marked lung injury occurs coughing is very troublesome.

Such patients, under ordinary analgesic medication, go through agonising paroxyms of pain during this reflex coughing. Patients on morphine and amiphenazole have none of these problems, cough freely and co-operate wholeheartedly with the physiotherapy staff.

It is accordingly felt that this drug combination is ideal for thoracic trauma—operative and otherwise.

Fractures: (67 *Cases aged* 20–60 *Years*). The injuries included fractured humeri, Colles' fractures, fractures of the pelvis, femur, tibia and ankle.

Except for cases with fractured femurs, all the other fractures were treated under the sole analgesic of morphine-amiphenazole. No anaesthetic was required.

More than 50% of cases experienced 100% pain relief from the injection and in only 2 cases was pain relief limited to 50%.

But for 2 patients who exhibited generalized sweating, no side effects were observed.

The respirations of one patient with a fractured olecranon dropped to 8 per minute, but were deep and full and no cyanosis was evident.

Dislocations: (8 *Cases Aged* 26–50 *Years*). Morphine-amiphenazole was given either as the sole medication or for post-operative relief of pain. Three patients with dislocated shoulders and 2 with dislocated elbows had their dislocations reduced under 1 unit of morphine-amiphenazole. No further analgesia was required. No side effects were observed with this series.

Spinal—Soft and Bony Injuries: (11 *Cases Aged* 25–45 *Years*). 70% of patients experienced 100% pain relief. The lowest amount of pain relief was experienced by 1 patient whose pain was only relieved 70%.

Two cervical spine subluxation injuries were put into Minerva plaster fixation whilst the spine was under traction from the ceiling. They received 1 unit of morphine-amiphenazole as a sole analgesic and the pain-free, co-operative patients were a great help during the procedure.

Burns: (13 *Cases Aged* 16–56 *Years*). The burns ranged in extent from 10% to 45% and were principally superficial.

The local treatment of these cases was:

(*a*) 1 unit morphine-amiphenazole as the sole analgesic.

(*b*) Cleaning of the burnt areas and removal of all debris and blisters.

(*c*) Frosting of the areas with penicillin-lactose powder.

(*d*) Spraying the areas with Nobecutane and a modified exposure therapy.[6]

The lowest degree of pain relief was 70% (3 patients). The other patients had relief of pain ranging from 80% to 100%. In this series, 2 cases exhibited generalized sweating. Both had only obtained 70% relief of pain.

One patient, aged 16 years, who had just finished a big evening meal before being burnt, vomited.

The doctors attending these cases agreed that morphine-amiphenazole afforded very great pain relief and that burn toilet under this procedure was practicable.

Soft Tissue Injuries: (39 *Cases Aged* 18–45 *Years*). All cases received morphine-ami-

phenazole as the sole analgesic agent. They included 24 patients with incised or lacerated wounds all over 2 inches long and at least 2 or more in number.

Of the 39 patients 31 experienced 100% pain relief. No side effects were experienced in this series.

Mandibular Injuries: (20 *Patients with One or More Fractures of the Mandibular Arch*). These were treated by interdental wire fixation after reduction. The sole analgesic was 1 unit of morphine-amiphenazole; all patients were conscious and able to co-operate during treatment. Only one patient complained of slight but bearable discomfort during the wiring. No side effects were experienced.

Hand Sepsis and Injuries: (65 *Patients Aged* 18–50 *Years*). These included 4 cases of amputations for hopeless digital sepsis, 20 cases of compound fractures and dislocations and 6 cases of traumatic amputation.

All received full treatment under 1 unit of morphine-amiphenazole as the sole analgesic, except for 2 cases which had gross pain. They were amputations for hopeless digital sepsis and required a supplementary anaesthetic of 0.25 g. Pentothal. In only 3 cases was the degree of pain relief as little as 60% and 2 of these had generalized sweating. No other side effects were experienced and both patients and doctors agreed that the operative procedures were feasible under morphine-amiphenazole analgesia.

Abdominal Conditions: (85 *Patients*). These include appendix disease, ano-rectal disease, visceral trauma, herniae, peptic ulcers and urethal conditions.

For pre-operative sedation, 1 unit of morphine-amiphenazole was given. Ischio-rectal abscesses were opened with morphine-amiphenazole as the only pain-relieving agent.

At no time during this series of abdominal surgical procedures was it felt that the clinical progress of the case was in any way masked, and the alert, pain-free patients were a great help, in contrast to the querulous, tortured patients who have been denied analgesia. All patients received morphine-amiphenazole during the post-operative phase with extremely satisfactory results. The morphine did not cause any intestinal problems; in fact, the distention was less, the bowel sounds returned earlier and the patients were ambulatory sooner than comparable cases without this therapy.

The only side effects noticed were in 9 patients whose pain relief was between 60–70% and who had generalized sweating.

SUMMARY

In the foregoing series 196 patients underwent minor surgical procedures with morphine-amiphenazole as the sole analgesic agent.

These comprised 20 thoracic injuries, 34 fractures, 5 dislocations, 3 spinal soft and bony injuries, 56 hand sepsis and injuries, 12 burns, 30 soft tissue injuries, 17 mandibular injuries and 19 abdominal conditions.

OBSERVATIONS WITH MORPHINE AND AMIPHENAZOLE AS THE SOLE ANALGESIC AGENT DURING MAJOR PROCEDURES

Angiography. It was felt that this type of analgesia might be the answer to the difficult problem of anaesthesia for angiography of circle of Willis aneurysms. Accordingly, 2 such cases were given morphine gr. 1 and amiphenazole 30 mg. 40 minutes before the commencement of the procedure. Some local anaesthetic was infiltrated around the point of carotid puncture to obviate spasm. Both patients were extremely co-operative and made no indications of discomfort until the contrast medium was diffusing through the main cerebral arteries—the hot pain of this broke through the pain barrier and the first film was spoilt by movement. However, the repeat film and those of the second case were successful, after the patients had understood what would happen and had received encouragement. Notwithstanding this, it was obvious that they did experience pain of some degree. This experiment was a disappointment and it was felt that morphine gr. 1½ may cover this obviously intense, very hot pain sensation.

MAJOR SURGERY

Amputations. Case A. This male patient, aged 90 years, was admitted in a very ill state with gangrene of the right leg, a mid-calf discharging wound and pus in the calf muscle planes. He was given 1 unit of morphine-amiphenazole for the extreme pain, slow blood transfusion, correction of fluid, sugar and electrolyte balance. After 48 hours he was judged fit for removal of the foul-smelling leg by above-knee amputation.

9.45 a.m. Pulse 108 and respirations 26 per minute. Blood pressure 80/50 mm. Hg. Morphine gr. 1 and amiphenazole 30 mg. given.

10.00 a.m. Pulse 132 per minute and respirations dropped to 5 per minute; cyanosis. Amiphenazole 25 mg. given.

10.10 a.m. Pulse 124, respirations 10 per minute, deep and adequate. No cyanosis.

10.40 a.m. Pulse 124, respirations 10 per minute. Operation begun. No reaction to the skin incision.
10.50 a.m. Pulse 124, respirations 10 per minute. Muscles cut. No reaction.
10.56 a.m. Pulse 150+, respirations 6 per minute. Sciatic nerve divided and the patient became very shocked.
10.58 a.m. Systolic 40/? mm. Hg. (cyanosed).
Intravenous Lethidrone 10 mg. / Intravenous Methedrine 15 mg. — Blood drip under pressure.
10.59 a.m. Blood pressure 105/50 mm. Hg.
11.15 a.m. Operation finished. Pulse 120, respirations 9 per minute. Blood pressure 92/50 mm. Hg. Patient shocked.
12.30 p.m. Patient moved off operation table to the Ward. Pulse 116, respirations 9 per minute. Blood pressure 94/50 mm. Hg. Condition much better.
1.30 p.m. Pulse 114, respirations 11 per minute. Blood pressure 102/55 mm. Hg. Better.
6.00 p.m. Generally better. Sitting up, light diet.
9.00 a.m. (Next morning). In good shape. No abnormal features.
9.40 p.m. Sleeping. Well.
3.30 a.m. Found dead in his sleep.

It was felt that the severing of the sciatic nerve broke through the pain barrier produced by the morphine-amiphenazole and caused the severe shock. Accordingly, in Case B, the sciatic nerve was infiltrated with a local anaesthetic before it was severed.

Case B. This was a male of 65 years with peripheral vascular disease resulting in gangrene of the left lower leg. Neglected infection of an ulcer on one toe had led to a massive infiltration up the muscle planes of the calf. He was very sick, malnourished, anaemic, toxaemic and dehydrated—a very poor operative risk; 24 hours were spent with general treatment, e.g. blood transfusion, hydration, invert sugar, alcohol, electrolytes, antibiosis, etc. The blood transfusion was continued during the operation.

It was decided to perform an above-knee operation. The patient was given morphine gr. 1 and amiphenazole 25 mg. intramuscularly at 10 a.m. The pulse rate was 100 per minute, respirations 32, blood pressure 90/60 mm. Hg.

At 10.25 a.m. the tourniquet was applied. At this stage the pulse rate was 104 per minute and respirations 12. The operation began at 10.35 a.m. and was completed at 11.05 a.m., during which time the pulse rate rose from 104 to 126 and respirations varied from 12 to 20 and were finally 10 when dressings were applied. At this stage the blood pressure was 110/70 mm. Hg. Throughout the entire procedure respirations were deep and adequate and there was no cyanosis.

The only adjunctive analgesic was the infiltration of the sciatic nerve with a local anaesthetic before it was severed. During the next 2 hours the pulse settled down to 94 and respirations to 10 per minute. At one stage respirations dropped as low as 6 per minute, but were deep and adequate with no cyanosis.

This pulse and respiratory frequency continued unchanged for the rest of the day and he was sitting out of bed in the evening. He did not remember anything about the operation nor did he complain of any subsequent pain. He made a very good recovery from the operation and unfortunately died from a coronary thrombosis some 3 months later.

Case C. This was a female, aged 16 years, who had had a tumour arising from the left metacarpo-phalangeal joint excised. It was found to be a malignant synovioma. Eight months later she reported with the whole hand expanded by tumour infiltration, with local lymph node involvement, excessive pain, anaemia, general body wasting, etc. She had not slept for days. One unit of morphine-amiphenazole gave pain relief for only about 6½ hours. After 48 hours' preparation, including blood transfusion, she was submitted to a high amputation of the arm.

9.00 a.m. Pulse 98 and respirations 24 per minute. Blood pressure 110/60 mm. Hg. Morphine gr. 1 and amiphenazole 30 mg. given.
9.15 a.m. Pulse 90, respirations 21 per minute. Blood pressure 110/60 mm. Hg.
9.30 a.m. Pulse 86, respirations 14 per minute. Blood pressure 110/60 mm. Hg.
9.40 a.m. Pulse 78, respirations 12 per minute. Blood pressure 110/60 mm. Hg. Operation begun. No response to gross painful stimuli.
9.50 a.m. Pulse 88, respirations 12 per minute Blood pressure 120/76 mm. Hg. Muscles cut. Patient agitated, probably not feeling any pain, but terrified at the idea of losing an arm.
Because of the patient's hysteria, 0.1 g. Pentothal was given. Patient sleeping, pulse 76, respirations 8 per minute. Slight cyanosis. Oxygen given for 1 minute, with rapid disappearance of cyanosis.
10.00 a.m. Pulse 74, respirations 10 per minute. Bone cut. No reaction of pain.
10.15 a.m. Pulse 76, respirations 10 per minute. Operation finished.
11.00 a.m. Pulse 76, respirations 10 per minute. Drowsing, no pain. No cyanosis.
6.00 p.m. Pulse 74, respirations 14 per minute. Completely awake, no pain.
Uninterrupted recovery. No further analgesia necessary.

After completing the series, our attention was drawn to a report[7] where a pethidine-amiphenazole combination was used as the sole analgesic agent for an abdominal operation in an 87-year-old moribund patient with a severe gastrostaxis. The operation lasted 2¼ hours, during which time the patient showed no response to painful stimuli and the post-operative course was completely uneventful.

The significant feature was the fact that no sedation was required until 12 hours after the operation.

CONCLUSIONS

These results indicate that the morphine-amiphenazole combination has an important place in the relief of acute pain comparable to the excellent results from the same therapy in cases of chronic, agonizing, inoperable malignant disease. The findings in the thoracic injuries series are particularly significant in this respect. The pain is relieved, the cough reflex is unimpaired, the brain stem centres are not depressed and early ambulation and co-operative physiotherapy are possible. Similar remarks apply in cases of burns.

The standard regime used for minor operative procedures will probably commend itself to practitioners working alone who wish to perform similar operations. Maximum analgesia (sufficient for operative procedures) occurred about 40 minutes after the intramuscular injection, and was followed by a period of comparable analgesia for 35–40 minutes. Testing of analgesia in most of the cases in the series by very severe painful stimuli confirmed these impressions. Thereafter, adequate analgesia to sustain the post-operative pain continued.

The dosage of morphine is certainly in excess of the maximum stated in the Pharmacopoeia, but the concomitant use of amiphenazole counteracts the dangers. Thus this regime is very much easier to the relatively uninitiated than is regional anaesthesia, and the antidote of more amiphenazole intravenously is just as easy, should any difficulties arise.

Major operations were performed under the analgesic influence of these drugs to add credence to its possibilities for minor operations, and to explore its potentiality as a substitute for more formal anaesthesia in very poor-risk cases. The major limb amputation cases described in the series can scarcely be considered as first class candidates for general anaesthesia. This analgesia has an important place in the management of this very sick group of patients.

(*a*) *Consciousness.* The general impressions gleaned from the preliminary trial were confirmed subsequently. However, the terminal dozing was of a catnap type and the patient was very easily roused to full alertness by slight stimuli, e.g. talking to him in a normal voice. Many of these observations were done when the other patients in the Ward were asleep. It was also a curious fact that, although the patient was awake, alert and responsive during operative procedures, the memory of current conversations was subsequently blurred or entirely absent.

(*b*) *Generalized Sweating.* A profuse generalized sweating occurred in 26 cases. It was often severe enough to necessitate a sponge-down and change of nightwear. It usually began about the time the injection was producing early analgesia and lasted for periods of ± 2 hours. It occurred in cases where analgesia was nowhere nearly complete, i.e. in the low-percentage pain-relief groups.

(*c*) *Muscle Twitching, Delirium, Cardiac Problems and Vomiting.* None of these possible side effects were encountered. The 2 patients who vomited did so for other more likely causes. The smooth treatment of the fractured mandibles (by interdental wiring fixation) under this analgesia contrasts with the fears of vomiting in such patients undergoing similar treatment under formal anaesthesia.

(*d*) *Constipation, Ileus, etc.* These did not occur as hazards of the therapy. In fact, it is considered that ileus was much less severe than in parallel cases. Audible bowel sounds, passage of flatus, etc. seemed to return earlier than usual. There were no cases of post-operative urinary retention.

(*e*) *Cyanosis and Respiratory Depression.* In the vast majority of the patients these complications were conspicuous by their absence. Adequate reference has been made to the female patient who had morphine and amiphenazole pre-operatively and curare during the subsequent formal anaesthesia.

Likewise, the male with the traumatic pneumo-haemo-thorax who was not given his covering dose of amiphenazole is also described.

The 90-year-old very sick male who underwent above-knee amputation for gangrene under morphine and amiphenazole probably owes his manifestation of these complications to accompanying shock. The male hernia repair and the female arm amputation patients both manifested their fleeting cyanosis after a supplementary small intravenous dose of Pentothal, suggesting that the addition of this known respiratory depressant, even in minute doses, may upset the balance of the morphine-amiphenazole equilibrium.

SUMMARY

This clinical investigation explores the usefulness of the combination of morphine and amiphenazole in the relief of acute surgical pain.

The results from 389 patients so treated are presented.

The combination was used as:

i. A post-traumatic analgesic agent.

ii. A post-operative analgesic agent.

iii. The sole analgesic agent during 196 minor operations.

iv. The sole analgesic agent during 5 major operations.

The results indicate the extreme efficacy and safety of this analgesic regime.

The Daptazole brand of amiphenazole used in this investigation was generously supplied *gratis* by Keatings Pharmaceuticals Ltd., the South African agents of A. & G. Nicholas Ltd., England.

The Acting Medical Superintendent of Baragwanath Hospital (University of Witwatersrand), Johannesburg, has kindly permitted the publication of this investigation which was carried out in the Hospital.

This investigation owes a great deal to the valuable and scientific work by Shaw and Shulman,[2] Shaw and Bentley,[3] McKeogh and Shaw,[4] and Hügin.[5]

OPSOMMING

Die doel van hierdie kliniese ondersoek was om vas te stel hoe nuttig 'n samestelling van morfien en amifenasool vir die verligting van akute chirurgiese pyn is.

Die resultate in die geval van 389 pasiënte wat op hierdie manier behandel is, word aangebied.

Die samestelling is gebruik as:

i. 'n Na-traumatiese pynstillende middel.

ii. 'n Na-operasie-middel vir die verdowing van pyn.

iii. Enigste pynstillende middel tydens 196 klein operasies.

iv. Enigste pynstillende middel tydens 5 groot operasies.

Die resultate bewys dat hierdie pynstillende behandeling besonder doeltreffnd en veilig is.

REFERENCES

1. Holmes, J. M. (1956): Lancet, **2**, 765.
2. Shaw, F. H. and Shulman, A. (1955): Brit. Med. J., **1**, 1367.
3. Shaw, F. H. and Bentley, G. A. (1952): Nature, **169**, 712.
4. McKeogh, J. and Shaw, F. H. (1956): Brit. Med. J., **1**, 142.
5. Hügin, W. (1956): Schweiz. Med. Woch., **30**, 1100.
6. Fleming, R. A. (1957): Med. Proc., **3**, 304.
7. Lurie, E. (1958): Med. Proc., **4**, 48.

ACUTE POLIOMYELITIS*

A STUDY OF THE CLINICAL MANIFESTATIONS OF FIFTY CASES

SEEN AT THE CHILDREN'S HOSPITAL, JOHANNESBURG, DURING THE 1948 EPIDEMIC

WITH SPECIAL REFERENCE TO THE MANAGEMENT IN THE ACUTE PHASE

J. L. BRAUDO, M.B., B.CH., M.R.C.P. (EDIN.)
Johannesburg

(*Continued from p.* 349)

IV. LABORATORY FINDINGS

The laboratory investigation conducted in this survey included cerebrospinal fluid and urine examinations in each case and full blood counts together with sedimentation rates in 24 of the 50 cases.

Cerebrospinal Fluid (*CSF*). Examination included measurement of the CSF pressure, determination of the number and type of cells per c.mm., protein and sugar estimations in each case.

The normal CSF *pressure* in children is between 60–90 mm. of CSF with the patient lying relaxed on his side. Pressures were recorded in 35 cases and ranged from 90 to 210 mm. of CSF. Normal figures were noted in 5 cases.

The normal CSF may contain up to 5 lymphocytes per c.mm., but neutrophils are not usually encountered. Peabody *et al.*[30] considered 10–12 cells per c.mm. as the upper limit of normal. The latter figure has been accepted by several workers.[52, 53] Cell counts above 12 per c.mm. were found in 46 cases and under 10 per c.mm. in 4 cases. Everyone in the latter group had at least 3 neutrophils per c.mm. and was therefore regarded as abnormal. The cells included 2 varieties, neutrophils and lymphocytes. The number of neutrophils in 20 cases was greater than the number of lymphocytes. Seventeen of the counts were recorded before the fifth day of the actual illness and 3 between the fifth and eighth days. Twenty-six showed an initial increase in lymphocytes over neutrophils. In this series, therefore, an excess of neutrophils as compared with lymphocytes in the initial counts taken before the fifth day of the ill-

* The References will be published at the end of the concluding article in this series.

ness was present in 17 cases and *vice versa* in 15 cases.

Chemical investigation comprised protein, sugar and chloride estimations in every case.

Protein Findings: The normal protein content in CSF ranges between 20 and 40 mg. per 100 c.c.[54] Figures above 50 mg. per 100 c.c. were regarded as abnormal. In this series the following results were obtained: 8 cases showed excessive protein in the CSF, 5 in the initial examination.

Sugar estimations were carried out in every case. The normal sugar content of the CSF ranges between 40 and 80 mg. per 100 c.c.[54] In 44 cases the figures were normal. Five cases showed figures between 80 and 100 mg. reaching 120 mgs. per 100 c.c. in one case. It is interesting that all the abnormal results occurred in the bulbo-spinal and bulbar groups. Three of the patients died, whereas one developed the raised sugar when she went into deep coma. The other 2 cases made good recoveries.

Colloidal gold curves were not obtained in these patients but are reported as luetic or meningitic in form,[59a] while the colloidal benzoin is frequently positive.[79] The results of CSF examinations in this series were very similar to those reported by other workers. The rise in cerebrospinal fluid pressure was in complete agreement with the reports in other epidemics. The cell counts showed a predominantly neutrophil response in 17 cases in the first few days of the disease, whereas other workers[30, 55] reported predominantly lymphocytic responses at this stage. A raised protein in the second and third weeks of the disease was a common finding.[56, 57] The findings in this series did not conform to that pattern.

It might be necessary to examine more than one sample of the CSF. This was well demonstrated in one case belonging to the non-paralytic group where examination on the first day of the disease was entirely normal, whereas a pathological cell count was found the next day. Nicholls[52] stressed the influence of the day of the disease on the CSF changes and the importance of repeating lumbar punctures in the detection of pathological changes. Eyre-Brook[56] said it might be necessary to examine more than one sample especially if the first was examined towards the end of the second week when the cell count had usually fallen to normal limits and the protein increase had hardly begun. Andelman *et al.*[57] confirmed the latter author's impression and stressed the rising protein content in the third and fourth weeks of the disease. Hence, the protein rise in the CSF was only consistently seen 3 weeks after the onset of the disease.

The sugar content of the CSF was usually normal.[52,53] The raised sugar findings in the cases belonging to the bulbar and bulbo-spinal groups might be attributed to lesions of the medulla in which glycosuria may be found.[53] However, none of our cases had glycosuria. Peabody *et al.*[30] reported a fatal case with excessive sugar in the CSF, but this finding has not been noted by other workers. Since poliomyelitis affects the medullary centres in both human fatal cases and the experimental animal, it seems reasonable to postulate that the raised CSF sugar is due to the extensive pathology in this region.

Finally, the question of the normal CSF in poliomyelitis is worthy of discussion. Although 4 cases in this series did not show an increase above 10 cells, the presence of at least 3 neutrophils in each instance should be regarded as abnormal. Normal findings in clinical and proven pathological cases in poliomyelitis have been well described. Fraser[58] reported a fatal case with a normal CSF. Kolmer *et al.*[59] stated that 23% of 609 cases had less than 12 cells in the CSF. Nicholls[52] recorded normal cytological and chemical findings in the CSF in 14% of 320 cases. A repeat examination in 24–48 hours in 13 normal cases in that series revealed a pathological number of cells. It was therefore evident that a normal CSF could be found at some stage in poliomyelitis, but the chances were greatly reduced when repeated examinations were made.

Blood Counts. Full blood counts on admission were performed in 24 (48%) of the total number of patients. Eleven cases belonged to the non-paralytic group, 7 to the bulbar and bulbo-spinal and 6 to the spinal paralytic. The haemoglobin and red cell estimations were normal in each case. The total white counts ranged from 6,300 per c.mm. to 19,000 per c.mm. Twelve cases showed a raised white cell count of 10–20,000 per c.mm. The percentage of neutrophils ranged from 25–84% of the total number of white cells and the lymphocytes from 19–71%.

In this series 11 cases had an increase in neutrophils, 8 an increase in lymphocytes and 6 cases a normal differential count.

Peabody *et al.*[30] found a constant and marked leucocytosis. In several instances the count was as high as 30,000 cells per c.mm.

Paul[60] stated that the white blood cell count during the acute stage was usually in the region of the 10,000–14,000 cells per c.mm. with 10–55% lymphocytes.

Sedimentation Rate (ESR). The sedimentation rate was measured according to the method of Wintrobe[60] in 24 cases. Seventeen cases had an ESR of 10 mm. or less in one hour while 7 cases had an ESR ranging from 12–45 mm. in 1 hour.

The normal figures for the ESR in children under 12 years of age is 0–10 mm. in 1 hour.[61] In this series, therefore, an elevated ESR was recorded in 7 cases, 3 of which belonged to the bulbar and bulbo-spinal group and 2 each to the non-paralytic and spinal paralytic groups, respectively.

SUMMARY

1. Lumbar taps were done in every case of poliomyelitis in this series. Pleocytosis in the cerebrospinal fluid was recorded in all cases. A few demonstrated albumino-cytologic dissociation. Elevated cerebrospinal fluid pressures were recorded in 30 of 35 cases measured. The highest pressures were noted in 3 bulbo-spinal cases, 2 of whom died. Six cases exhibited raised sugar levels. Three of these died and one went into deep coma. Normal cerebrospinal fluid findings have been recorded in acute poliomyelitis.

2. Full blood counts and ESR determinations were carried out in 24 cases. The white cell count may be normal or show a neutrophil or lymphocyte leucocytosis; 17 of 24 patients had a normal ESR.

3. Electrocardiograms were available in 8 cases. All the tracings were normal, but changes have been frequently described. They comprise P and T wave changes, arrhythmias and first degree heart block.

OPSOMMING

1. Lumbale aftappings is gedoen in iedere geval van poliomiëlitis in hierdie reeks. Pleositose in die serebrospinale vloeistof is in alle gevalle waargeneem. 'n Paar het albumino-sitologiese dissosiasie geopenbaar. Verhoogde serebrospinale vloeistofdruk is aangeteken in 30 van die 35 gevalle wat ondersoek is. Die hoogste druk is aangeteken by 3 bulbêre-ruggraat-pasiënte, twee van wie later oorlede is. Ses gevalle het 'n verhoogde suikerpeil getoon. Drie van hulle het gesterf, en een het in 'n diep koma geraak. Normale serebrospinale vloeistofbevindings is aangeteken in gevalle van akute poliomiëlitis.

2. Volle bloedtellings en vasstellings van die rooibloedsel-sedimentasie-tempo is in 24 gevalle uitgevoer. Dit witbloedseltelling kan normaal wees of 'n neutraal-kleurstofvattende of limfosiet-leukositose openbaar. By 17 van die 24 pasiënte was die rooibloedsel-sedimentasie-tempo normaal.

3. Elektrokardiogramme was in 8 gevalle beskikbaar. Al die natrek-tekenings was normaal, maar veranderings is al dikwels beskryf. Hulle bestaan uit P- en T-golfveranderings, arrhythmieë en hartblokkades van die eerste graad.

(To be continued)

COMPENSATION FACTOR IN LOW BACK INJURIES*

EDWARD M. KRUSEN, M.D.

and

DOROTHY E. FORD, M.D.

The histories of 509 patients treated for low back injuries were studied for differences that might be related to compensation. Only 55.8% of the 272 patients receiving compensation were rated as improved at the time of discharge, as compared with 88.5% of the 237 patients not receiving compensation. Over two thirds of the patients who did not receive compensation had appeared for treatment during the first month of symptoms, whereas only about one half of the patients who received compensation had been seen at this point.

The mean number of treatments received by the compensation group, both men and women, greatly exceeded that for the non-compensation group. Some patients in the compensation group responded well to conservative treatment and returned to their jobs after a minimum number of treatments; but in others there appeared to be a difficulty within the basic personality structure. Psychiatric experience with the latter type has not been encouraging. Throughout the study, the women expecting compensation showed the worst response to treatment while receiving the greatest number of treatments. Prompt, adequate diagnosis and early conservative treatment are

* Extracted from *The Journal of the American Medical Association*, **166**, 1128. (8 March 1958.)

recommended as essential in handling these patients, but there is real need for further investigation of the problem.

Results show that the longer a patient waits before treatment the smaller is the probability of his improving, regardless of whether he expects compensation or not, and that generally the patients who receive compensation are referred for treatment later than those who do not. The reasons for this are hard to explain. Admittedly, the more severely injured patients are eventually hospitalized for an intensive treatment programme, but one gets the impression that many of these patients receive inadequate therapy for a prolonged period of time. Even when an attempt is made to give physical therapy, this frequently consists of application of heat from a heat lamp or diathermy machine alone. This is certainly not adequate, but the patient considers it to be 'physical therapy' and, when he is finally referred for more intensive treatment, he has developed a prejudice against physical therapy which must be overcome.

From this standpoint, it would often be preferable if these patients received no treatment rather than inadequate therapy, and certainly the latter should not be continued over prolonged periods of time. Otherwise, many patients become extremely resentful toward their employers, their doctors, or both, and lose their motivation to return to work. If a doctor is treating a patient without being able to provide an intensive treatment programme, there appears to be a danger point at about one month, after which results of treatment fall off sharply for patients in the compensation group.

Although results are worse for patients who are referred for treatment after 3 months or more, it is usually still advisable to give them a trial of adequate treatment, since it has been shown that over one third of them can be improved sufficiently to return to work. Of course, if the same treatment could be provided within the first week after injury, almost twice as many would recover. Providing the patient with early treatment is especially important if he is receiving compensation. The earlier an accurate diagnosis about the need for possible surgery can be obtained, the easier it becomes to treat the patient.

Although there may be no ideal treatment time, we feel from our clinical impressions that a series of 18 treatments or a period of 3 weeks' intensive care, including bed rest and adequate physical therapy, constitutes a fair trial of conservative management. A patient who does not get any relief from these measures during that period should be reviewed with considerable concern. He probably requires surgery, or perhaps his psychological problems are so fixed that little help can be expected from further treatment.

In regard to physical therapy, this often can do more than directly affect the injury. Adequate physical therapy can provide an 'out' for the patient's psychological problems, if it is started early enough and carried out properly. It is well to encourage this effect by the general approach to the patient. Such an approach consists of maintaining from the outset the attitude that the back disability is only temporary and of recommending early settlement of the case. It appears that one can safely recommend early financial settlement to the patient, with provision for surgery if it be needed, since the passage of time does not greatly change the results of formal physical therapy. It might be advisable to stress that 'early' settlement refers to prompt settlement after diagnosis and a fair trial of adequate treatment, and not to settlement immediately after the injury.

It is interesting to note that the women expecting compensation have shown the worst response to treatment, while receiving the greatest number of treatments. Apparently, many resent that they are required to hold a job, and there seems to be no motive for the women with compensable back injuries to return to work. The compensable back injury is so common and its economic implications are so far-reaching that there is real need for further investigation.

OPSOMMING

Die beginsels wat toegepas behoort te word by die behandeling van pasiënte met beserings laag in die rug wanneer 'n skadevergoedingsfaktor by die saak betrokke is, word bespreek.

Die rol van fisiese en moontlike chirurgiese terapie word geëvalueer, veral vir sover dit betrekking kan hê op die vroeë beslegting van sodanige gevalle. Dit beteken vinnige uitbetaling na diagnose en nadat doeltreffende behandeling aan 'n billike toets onderwerp is, en nie uitbetaling onmiddellik na die besering nie.

Vrouens wat skadevergoeding verwag, ontvang die grootste aantal behandelings, maar toon die swakste reaksie hierop.

Die rugbesering waarvoor vergoeding betaalbaar is, is so 'n gewone verskynsel, en die ekonomiese implikasies daarvan is so verreikend dat daar 'n werklike behoefte aan verdere ondersoek bestaan.

G. M.

MALARIA CONTROL IN SOUTH AFRICA

HOW DOES THE CHANGING STRATEGY IN MALARIA CONTROL AFFECT US?

KARL HECHTER-SCHULZ
Johannesburg

Recently Pampana (1954) set the question of whether the time had arrived to change the general strategy of malaria control as practised universally to-day. Since the introduction of DDT, about 10 years ago, revolutionized the technique of malaria control and made the protection of millions of inhabitants of malarious areas possible, we have been faced with the problem of the same control measures having to be repeated year after year, involving recurrent expenditure pegged at a very high level. Although the expenditure has made possible the development of land formerly valueless and increased human well-being beyond our former reach, the time has now come to examine the possibility of evolutionary Nature compensating its creatures against the onslaught of Man, as manifested by vectors developing resistance against the residual insecticides being used, or by adopting a changing behaviour pattern in order to survive. In order to arrive at a stage where actual control work can be reduced, with a consequential reduction in expenditure and without involving a health hazard, malaria transmission must have ceased over a great geographical area, due either to a reduction in vector density or in a dying out of plasmodium parasites in infectious form. The vectors should not show any adaptation to the now conventional method of control, either by development of insecticidal resistance or by behaviour intended to avoid contact with toxic surfaces, before this happens.

Pampana has outlined the criteria which must be met before such a change in malaria strategy can take place. Two main conditions must be considered in order to evaluate the results of our malaria control programme—

1. The factors which affect a possible reduction of the residual insecticide spraying campaign; and

2. The possible development of resistance in our local vectors.

These criteria are enumerated and discussed with regard to local conditions in the text which follows.

I. THE FACTORS WHICH AFFECT A POSSIBLE REDUCTION OF THE RESIDUAL SPRAYING CAMPAIGN

1. *Every locality where transmission is possible should be under control.* Since the commencement of malaria control by means of residual insecticides in the Union of South Africa, ever-increasing areas have been covered by the campaign. Within a few years the majority of endemic areas were under control, commencing with the hyperendemic areas, until to-day more than 50,000 square miles in the Transvaal and about 10,000 square miles in Natal are under control. To-day about 2,000,000 persons of all races are directly protected yearly against the ravages of malaria, by the use of residual insecticides.

TABLE 1: NUMBER OF PERSONS DIRECTLY PROTECTED AGAINST MALARIA IN 1954

Transvaal		*Natal*			
White	*Bantu*	*White*	*Indian*	*Bantu*	*Total*
120,000	1,250,000	17,000	65,500	518,000	1,970,500

This, however, does not include all of the areas where malaria transmission is possible. Some marginal areas of low endemicity and a very few areas such as Upington, where malaria transmission dies out due to lack of a suitable vector, only to be reintroduced periodically when climatic conditions make vector breeding possible, receive attention only when epidemics threaten. Other areas which cannot be included in annual routine control campaigns are some marginal areas which are inaccessible at critical times of the year. The malaria control organization of the Union Health Department co-operates with its neighbours, and by agreement carries out control measures in one of the neighbouring territories along its borders.

Although vast areas are under control to-day there are a few foci left untouched, either from the commencement of the DDT epoch, or which have only periodic control measures applied to them. If the present control measures,

i.e. interhouse spraying with DDT and BHC were interrupted at present, these uncontrolled foci would act as centres from which vectors and plasmodium would be reintroduced.

2. *The assessment of results should be so organized as to make it possible to ascertain if and where a total interruption of malaria transmission has been attained.* Very fine results have been obtained in the decade of large-scale control, but nowhere can it be said that malaria transmission has been completely eradicated. The transmission has been interrupted over vast areas within the African sub-continent where it is most difficult to operate a successful public health organization, but, when climatic conditions were exceptional, we have witnessed a recrudescence of epidemic malaria in areas where it seemed that control had been firmly established. The rainfall during the malaria season for 1952-53 was exceptionally heavy, favouring a high mosquito density even in controlled areas, while floods and extensive rainwater pools made possible the extension of vectors into areas from which they are normally absent.

The density of vectors found in ratio to huts searched in the Transvaal fell from 1:9.9 in 1947-48 to 1:139 in 1951-52, only to rise again in 1952-53 to 1:25.

With an increase in vector density in 1952-53 came increased malaria transmission. About 2,000 positive blood slides were examined in the Transvaal and Natal in that year, compared with 84 examined the year before. Malaria cases hospitalized in 1952-53 were 2,409 for the 2 Provinces. The situation returned to normal the following year, when there was a vector density in the Transvaal of 1:208, and when 100 blood slides were examined and found positive.

The machinery within the Health organization used to assess the results of years of control work is not delicate enough at present to forecast the possibility of epidemic transmission within control areas in times of excessively favourable vector conditions. The control organization would be in a better position to assess when control measures can be suspended

TABLE 2: VECTORS FOUND IN CHECK SPRAYING OF HUTS IN THE TRANSVAAL

	Number of Huts Sprayed	*Vectors Found*	*Vector Ratio per Hut*	*State of Rainfall*
1947–48	178,754	18,035	1:9·9	Particularly wet
1948–49	132,035	12,652	1:10·4	Normal
1949–50	211,899	8,285	1:25·6	Dry
1950–51	168,812	1,572	1:107	Dry
1951–52	157,063	1,133	1:139	Particularly dry
1952–53	145,219	5,806	1:25	Very wet
1953–54	149,911	716	1:208	Normal
1954–55	170,763	3,512	1:48·6	Wet

TABLE 3: BLOOD SLIDES EXAMINED IN THE TRANSVAAL*

Year	*Total Examined*	*Number Positive*
1939–40	10,312	4,494
1940–41	6,544	4,287
1941–42	9,514	4,498
1942–43	5,994	2,396
1943–44	6,713	3,980
1944–45	5,151	1,381
1945–46	2,938	1,263
1946–47	1,898	348
1947–48	786	441
1948–49	945	128
1949–50	453	51
1950–51	306	41
1951–52	242	19
1952–53	1,658	700
1953–54	518	104
1954–55	723	251

* The slides examined before 1947-48 represent a fraction of all malaria cases occurring, whilst those examined after this date include practically all suspected cases of malaria in the Transvaal.

TABLE 4: SUSPECTED MALARIA CASES HOSPITALIZED IN THE TRANSVAAL

Year	*Number of Cases*
1942–43	2,079
1943–44	1,909
1944–45	1,440
1945–46	1,177
1946–47	601
1947–48	507
1948–49	454
1949–50	263
1950–51	142
1951–52	61
1952–53	790
1953–54	87
1954–55	255

or have to be reintroduced if a specialist team of entomologists and malariologists were appointed to evaluate conditions in the field constantly.

3. *Malaria control should be implemented with the greatest thoroughness, at one time and in as large an area as possible, bordered by areas where naturally or as a result of control there is no transmission.* The technique of malaria control used is that first demonstrated by de Meillon and Park Ross in Natal in the early thirties to be effective in controlling malaria transmission by the reduction of vector species, i.e. inter-domiciliary spraying with insecticides. Only improved apparatus and the modern residual insecticides are now used, adapted from methods developed in other countries which pioneered this form of malaria control.

Mostly adulticides are used with some larvicidal work proceeding in the known hibernating areas. Chemo-prophylaxis is not practiced, but mass therapy with quinine was carried out in the past through magistrates and native commissioners.

TABLE 5: QUININE USED IN TRANSVAAL DURING THE YEARS 1943–44 TO 1953–54

Malaria Season	*No. of 5 gr. Quinine Tablets Used*
1943–44	2,000,000
1944–45	1,478,000
1945–46	1,298,000
1946–47	677,000
1947–48	300,000
1948–49	217,000
1949–50	151,000
1950–51	94,000
1951–52	40,000
1952–53	82,000
1953–54	3,000
1954–55	11,500

DDT has been used for a considerable period while the use of BHC has increased over recent years. DDT emulsion and a small quantity of malarial oil is still used for larviciding. In the Transvaal the following materials were used:

	1954–55	1953–54
Malarial oil 44 gallons	201	469
5% DDT (Paradex) gallons	15,263	10,363
27½% DDT emulsion gallons	4,147	3,009
40% BHC wettable powder lbs.	168,649	141,434

The total number of huts sprayed with DDT rose from 346,601 in 1947-48 to 605,419 in 1952-53.

TABLE 6: HABITATIONS SPRAYED DURING THE PERIOD 1947–48 TO 1953–54

Year	*Transvaal*	*Natal*
1947–48	281,907	64,694
1948–49	329,494	49,373
1949–50	429,537	108,930
1950–51	356,819	106,930
1951–52	320,785	66,897
1952–53	414,787	190,632
1953–54	287,566	191,881

The cost of malaria control in the Transvaal alone rose from £49,000 in 1944-45 to a maximum in 1947-48 of £396,000 and fell again to £165,000, around which figure it has remained for several years. The cost of directly protecting the community exposed to malaria infection is about 2s. 6d. per person per annum.

The dosage recommended at the Malaria Conference in Equatorial Africa for the control of the main vectors in Africa South of the Sahara, is 2.2 g. of the para'para isomer of DDT per square metre every 6 months. The transmission period here is about 4 to 6 months, and while no absolute dosage figure can be stated at the moment it can be considered that this approaches the recommendation made above.

Species and varieties of malaria vectors in Africa found infected in nature have been listed by de Meillon as follows:

1. *austeni*
2. *brunnipes*
3. *christyi*
4. *concolor*
5. *coustani coustani*
6. *coustani* var. *ziemanni*
7. *demeilloni*
8. *domicolus*
9. *flavicosta*
10. *funestus funestus*
11. *funestus* var. *imerinensis*
12. *gambiae gambiae*
13. *gambiae* var. *melas*
14. *hancocki*
15. *hargreavesi*
16. *implexus*
17. *maculipalpis*
18. *marshalli* var. *gibbinsi*
19. *michaeli*
20. *moucheti moucheti*
21. *moucheti* var. *nigeriensis*
22. *nili*
23. *obscurus*
24. *paludis*
25. *pharoensis*
26. *pretoriensis*
27. *rhodesiensis*
28. *rufipes*
29. *squamosus*
30. *walravensi*

Of these we are most concerned with *funestus funestus* found east of the Drakensberg escarpment and *gambiae gambiae* which occurs throughout the malarious areas where breeding conditions are good, and permanently in frost-free places.

Control in the Union of these two important African vectors has been shown to be efficient by the present technique used during years with normal rainfall. When conditions were

exceptionally favourable for *gambiae* propagation control measures have been severely taxed.

The present technique has been efficient enough to interrupt the transmission of malaria in years of ordinary rainfall, but with increased opportunities for vector breeding in *gambiae* areas there has been a threatening return of transmission in epidemic form. On the evidence of past years it can be taken that both vectors and plasmodium infiltrate back into controlled areas in such years from the inaccessible foci left uncontrolled.

4. *Appropriate safeguards should be introduced to ensure rapid detection of every case of malaria and prompt elimination of possible transmission.* The time has come for consideration of a further possible change in the present strategy of malaria control in the Union to consolidate the gains made and to prevent at all costs a recurrence of transmission in the former malarious areas.

A surveillance service should be developed similar to that already operating in other countries, i.e. Greece, U.S.A. This surveillance service should operate throughout the controlled areas to detect signs of any reinfection and to take appropriate action without delay. Determination of vector densities and malaria incidence will be the primary task of this service.

Two services should be established within the framework of the present organization. One would be the present control organization and the other should be composed of several mobile specialist teams of malariologists, entomologists and malaria engineers whose task would be the demarcation of areas in which control could be discontinued and the detection and control of possible sources of reintroduction of the infection in these areas.

II. POSSIBLE DEVELOPMENT OF RESISTANCE IN OUR LOCAL VECTORS

1. The second point of discussion on the possibility of changing strategy raised by Pampana, that of the development of resistance, must be very carefully considered. A high degree of resistance* would interfere with control of malaria transmission while changes in behaviouristic pattern need not necessarily do so. Have our vectors developed resistance to the chlorinated hydrocarbons used in this country for their control? Have they developed a new behaviouristic pattern calculated to circumvent control, and if so has malaria transmission been affected by such a changing pattern?

2. To the first query we cannot at the moment give a satisfactory reply as work on testing resistance of local vectors has had to be discontinued for the present owing to the onset of winter conditions. However, work done in other countries which shows varying degrees of vector resistance to residual insecticides cannot be ighored.

TABLE 7: SOME VECTOR RESISTANCE REPORTED FROM ELSEWHERE

Country	*Vector*	*Author*
U.S.A.	A. quadrimaculatus	
Greece	A. Maculipennis*	G. Belios
	A. superpictus*	G. Belios
	A. sacharovi	Livados
Lebanon	A. sacharovi	C. Garrett-Jones, G. Grani
Indonesia	A. sundiacus	
Saudi Arabia	A. Stephensi	
Panama	A. albinanus (behaviouristic)	

* Recently reported as having slight resistance.

3. The second query posed on the behaviouristic pattern of at least one of the vectors is easier to answer. In the case of *gambiae* doubt has been thrown on the possibility of its effective control by means of DDT since Muirhead-Thompson's experiment in West Africa pointed to a possible irritant effect on *gambiae melas* by this insecticide, which hindered contact with toxic surfaces.

4. A further factor of uncertainty is introduced by the type of formulation of DDT used on various kinds of surfaces. It is now known that toxicity is lowered at the surface not only by porosity but also by the chemical composition of the materials used in the construction of walls. When wall surfaces are porous these absorb most of the insecticide, and when oil solutions are used only about 5% of the original amount may be available on the surface as a toxic layer to insects coming in contact with insecticides such as DDT and Dieldrin which have no fumigant action. This represents a disadvantage which can only be overcome either by using water suspensions or increasing the dose of the insecticide. Insecticides which have fumigant properties such as BHC or aldrin are not so much affected,

* Resistance is defined by the symposium on the Control of Insects held in Rome in 1953 as the development of an ability in a strain of an insect to tolerate doses of toxicant which would prove harmful to the majority of individuals of a normal population of the same species. The term behaviouristic resistance describes the ability to avoid a dose which would prove harmful.

although suspensions in this case are also more desirable. It has been established that there is increased absorption in laterite soils containing iron oxide and alumina oxide which will inactivate to a relative degree any insecticide sprayed on the surface.

5. It has been shown by many writers from the time of Ronald Ross that it is not necessary to eradicate a malaria vector in order to obtain control of transmission. The work of Park Ross and de Meillon in South Africa showed that the density of the local vectors had to be reduced but slightly for control to be established. MacDonald has drawn attention to life expectancy of the vector as a factor in transmission in addition to density of vectors.

Density and life expectancy can be related when considered from the point of view of control programmes using residual insecticides. With a reduction in density comes a falling off of the mathematical chances of transmission, while a short life expectancy eliminates the possible maturation of the parasite cycle in the mosquito. MacDonald considers that a minimum maintained-mortality rate of between 60% and 70% per day is needed, but he considers that moderate exophilism would upset this target, unless very potent insecticides were used.

The time that a mosquito is in contact with a toxic surface will generally determine not only the mortality rate but also the time this takes. Davidson and Haddaway and Barlow have shown some irritant effect on mosquitoes by DDT, BHC and Dieldrin. DDT had the most irritant effect, next came BHC, while the longest contact times and highest mortality rates were recorded with Dieldrin. The choice of insecticide to be used is of vital importance in obtaining the objective of total malaria eradication.

6. De Meillon stated as far back as 1935 that the pattern of *gambiae* behaviourism can be expected to change over large geographical areas, and that possibly exophilic and zoophilic varieties existed, although more recent work shows that *funestus* has a high degree of anthropophilism and endophilism (precipitin tests for both species show about 70% positive for human blood in huts shared with animals).

The possibility of outdoor transmission cannot be overlooked. Available evidence from Natal and the Transvaal shows that this is a factor to be reckoned with as natives are in the habit of spending the night outside huts during summertime. During the transmission season of 1953-54 in the Transvaal fully 25% of all vectors searched for and caught were found outside human habitations. The figures for 1952-53 and 1954-55 are 12.5% and 40% respectively. Precipitin tests showed they had fed on humans. The places they were recovered from were the eaves of huts, animal habitats and cut banks of rivers.

Another problem to be considered is that of the changing use of agricultural land. In the Eastern Transvaal great increases in rice culture have been made, while extensive irrigation schemes are under construction.

This hydrographic factor must be considered here, as not only does it increase the total water surface available for *Anopheline* breeding already present, but may also result in the establishment of other vectors not yet found in the region, such as *funestus* var *imerinensis* which breeds extensively in Madagascar in rice fields and inundated flats and is regarded as a vector of some importance there.

DISCUSSION AND CONCLUSIONS

When considering the changing strategy of malaria control we are struck by the necessity of eradicating malaria transmission in as short a time as possible in order to bring down the costs of recurrent campaigns, and also to reduce the possibility of resistance or changing behaviouristic patterns of vectors from developing before cessation of transmission is brought about. In the one instance the advantage is one of economy, but in the other it is an urgent public health necessity. Should physiological or behaviouristic resistance develop before the elimination of plasmodium from the local malarious areas, then we will be faced with the situation as it existed before the advent of residual insecticides when very little could be done to protect people from the scourge of infection. On the other hand should resistance in the vectors come about after elimination of plasmodium then it will be of no importance.

Can we eliminate plasmodium entirely from our present malarious areas? Consideration of all the previous discussion shows how far we have progressed in this direction, but also clearly indicates how difficult it is going to be to eradicate malaria entirely. However, with an intensification and improvement of present techniques using more powerful insecticides, with the use of mass therapy with modern anti-malarials, particularly the more potent schizonticides and gametocides for eradication of plasmodium from carriers and with the full

co-operation of neighbouring States, this goal may eventually be achieved.

To bring about such eradication we must apply ourselves to the problems presented in our part of the African sub-continent. These can be summarized as follows:

1. Every locality where transmission is still possible should be vigorously treated both by residual adulticides and anti-malarials. Even areas of low endemicity or where transmission is only cyclic must receive constant attention. Where endemic areas cannot be reached by ordinary means of transport, helicopters and other aircraft might be used for transport and larviciding. These means have been successfully employed for the total eradication of Tsetse fly in the Union, in the most inaccessible areas.

2. Assessment of results of our control programme should be made by teams of malariologists, entomologists and malaria engineers carrying out research constantly within the malarious areas as a prelude to changing strategy. Three such mobile teams would suffice to cover all these areas, afterwards taking on the part of a surveillance service. The present organization functions satisfactorily as a control unit, and can be extended to make malaria eradication an established fact.

3. At the time of the introduction of residual insecticides into malaria control it seemed sufficient that the vector should be controlled, not necessarily eradicated. The eradication of mosquito vectors of disease has been attempted from Cyprus, Sardinia, Egypt and Brazil, by means of adulticidal methods assisted by other means of species sanitation. In all these instances there have been geographical barriers against reintroduction of the species from neighbouring areas. The Union, however, forming as it does part of the great African continent, can hardly hope that the total and permanent eradication of the vector species will be achieved in the foreseeable future, nor is this actually necessary for the purpose we have in mind, i.e. malaria eradication. We need only reduce the density and life expectation of the vector below the transmission threshold for a number of years. We are faced, however, with the possibility of physiological or behaviouristic resistance of the vector, so that in order to reduce vector densities as soon as possible continuous research should proceed on the suitability of the insecticides being used.

4. Treatment of the plasmodium carrier should be carried out at the same time to reduce the actual source of infection to a minimum regardless of what is happening to the vector. In this regard mass therapy under medical supervision using the proved antimalarials with high schizonticidal and gametocidal action should be instituted as soon as possible.

5. Co-ordinated action by neighbouring territories on both sides of their common boundaries would greatly assist in preventing spread of the disease into areas from which it had been eliminated. Such action is essential for the success of any widespread malaria eradication campaign.

What will the justification be for pushing up the price of present control in order to realize eradication of malaria from our country? For nearly a decade now we have spent an average of about £200,000 per annum, with the prospect of continuing to do so indefinitely under present conditions. If eradication cost twice this figure annually for a limited number of years with a considerable drop in expenditure after the target has been reached, then this would be a proposition economically worth while.

OPSOMMING

By die oorweging van die veranderende strategie van malariabeheer word ons getref deur die noodsaaklikheid om die verspreiding van malaria so gou doenlik te voorkom, want alleen dan sal dit moontlik wees om die koste van wederkerende veldtogte te verlaag, of die moontlikheid te verminder dat weerstandskragtigheid of veranderende gedragspatrone by draers ontwikkel voordat die oordrag van die siekte gestaak kan word. In die een geval bring dit ekonomiese voordele mee, en in die ander is dit 'n dringende openbare gesondheidsnoodsaaklikheid. Indien fisiologiese of gedragsweerstandskragtigheid ontwikkel word voor die uitroeiing van plasmodium in malariagebiede, sal ons van aangesig tot aangesig te staan kom voor die posisie wat in swang was voor die koms van insekvergifte met 'n nablywende effek, toe baie min gedoen kon word om mense teen infeksie te beskerm. As weerstandskragtigheid by draers daarenteen ontwikkel word ná die uitskakeling van plasmodium, sal dit van geen belang wees nie.

Kan ons plasmodium heeltemal uitroei in ons huidige malariagebiede? 'n Oorweging van alle vroeëre besprekings toon aan hoe ver ons reeds in hierdie rigting gevorder het, maar dui ook duidelik aan hoe moeilik dit gaan wees om malaria heeltemal uit te roei. Met die verskerping en verbetering van die huidige tegniek waar gebruik van kragtiger insekvergifte gemaak word, en deur die toepassing van massa-terapie met moderne malariabestrydingsmiddels, veral die kragtiger skisontisiede en gametosiede vir die uitroeiing van plasmodium in draers en met die volle medewerking van naburige state, kan hierdie doelwit uiteindelik bereik word.

Om sodanige uitroeiing te bewerkstellig, moet ons ons toelê op die oplossing van die probleme in ons deel van die vasteland van Afrika. Hulle kan soos volg saamgevat word:

1. Iedere gebied waar oordrag nog moontlik is, moet kragdadig met insekvergifte met 'n nablywende effek sowel as met malariabestrydingsmiddels behandel word. Selfs gebiede met 'n lae endemisme, of waar oordrag slegs siklies geskied, moet ononderbroke aandag geniet. Waar endemiese gebiede nie met die gewone vervoermiddels bereik kan word nie, sal dit miskien moontlik wees om gebruik van helikopters en ander vliegtuie te maak vir vervoerdoeleindes en die vernietiging van larwes. Sulke middele is reeds met welslae toegepas vir die algehele uitroeiing van die tsetsevlieg in die mees ontoeganklike dele van die Unie.

2. Die evaluasie van die resultate van ons beheerprogram moet toevertrou word aan 'n span malarioloë, entomoloë en malaria-ingenieurs wat ononderbroke navorsing in die malariagebiede moet doen as voorspel tot strategieverandering. Drie sulke reisende spanne sal voldoende vir al hierdie gebiede wees, en daarna kan die spanne in 'n toesighoudende diens omskep word. Die huidige organisasie funksioneer bevredigend as beheereenheid, en kan uitgebrei word om malaria-uitroeiing 'n voldonge feit te maak.

3. Toe insekvergifte met 'n nablywende effek vir die eerste keer vir die bestryding van malaria gebruik is, het dit geskyn asof dit voldoende sou wees om die draer te kontroleer en nie noodwendig om hom uit te roei nie. Die uitroeiing van muskiete wat siektes oordra, is aangedurf in Siprus, Sardinië, Egipte en Brasilië deur middel van metodes vir die vernietiging van volgroeide musikiete, aangevul deur ander muskietsoort-sanitasiemetodes. In al hierdie gevalle was daar aardrykskundige verskansings wat die her-invoering van muskiete uit naburige gebiede verhinder het. In die Unie wat deel van die groot vasteland van Afrika uitmaak, kan ons skaars hoop dat die algehele en blywende uitroeiing van die draersoorte in die voorsienbare toekoms bewerkstellig sal kan word. In werklikheid is dit ook nie nodig vir die doel wat ons voor oë het nie, nl. die uitroeiing van malaria. Al wat ons hoef te doen, is om die digtheid en die lewensverwagting van die draers vir enkele jare tot benede die oordragpeil te verminder. Die moontlikheid van fisiologiese of gedragsweerstandskragtigheid aan die kant van die draer moet egter in gedagte gehou word. Om draer-digtheid so gou moontlik te verminder, is dit derhalwe noodsaaklik dat ononderbroke navorsing gedoen moet word na die geskiktheid van die insekvergifte wat ons gebruik.

4. Die behandeling van die plasmodiumdraer moet terselfdertyd geskied om die werklike bron van infeksie tot 'n minimum te beperk, ongeag wat met die draer gebeur. Wat dit betref, behoort massa-terapie onder mediese toesig, met gebruikmaking van bewese malariabestrydingsmiddels met 'n kragtige skisontisied- en gametosied-effek, weer so gou moontlik ingestel te word.

5. Gekoördineerde optrede deur aangrensende gebiede aan weerskante van hul gemeenskaplike grenslyn sal veel bydra tot die voorkoming van die verspreiding van die siekte na gebiede waar dit reeds uitgeroei is. Sodanige optrede is noodsaaklik vir die welslae van enige wydverspreide veldtog vir die uitroeiing van malaria.

Watter regverdiging is daar vir die verhoging van die koste van die huidige beheermaatreëls om die uitroeiing van malaria 'n voldonge feit in ons land te maak? Gedurende byna 'n dekade het ons gemiddeld £200,000 per jaar uitgegee, en onder die huidige omstandighede is daar 'n sterk moontlikheid dat ons 'n onbepaalde tyd lank sal moet voortgaan om dit te doen. As uitroeiing gedurende 'n beperkte aantal jare twee maal soveel per jaar kos, en as die uitgawes dan aansienlik sal daal nadat ons ons doelwit bereik het, is dit 'n plan wat, uit 'n ekonomiese oogpunt, beslis die moeite werd sal wees.

This paper was written for presentation to the Malaria Conference, Pretoria, 1956, when the author was on the staff of the Plague Research Laboratory attached to the South African Institute for Medical Research, Johannesburg.

Thanks are due to the Secretary for Health for his kind permission to submit this paper for publication.

REFERENCES

de Meillon, B. (1951): *Species and Varieties of Malaria Vectors in Africa and their Bionomics*, W.H.O. Bull., **4**, 419.

MacDonald, G. and Davidson, G. (1953): *Dose and Cycle and Insecticide Applications in the Control of Malarie*, W.H.O. Bull., **9**, 785.

Pampana, E. J. (1954): *Changing Strategy in Malaria Control*. W.H.O. Bull., **11**, 513.

Union Health Department (1947–55): *Annual Reports*.

NOTES AND NEWS : BERIGTE

Mr. David A. Muskat, Ch.M., formerly in practice at 304 Pan Africa House, Johannesburg, has moved to new premises at 504 Medical Arts Building, corner Troye and Jeppe Streets, Johannesburg, *Telephone*: 22-9208.

* * *

Mr. C. A. R. Schulenburg, F.R.C.S., has returned from a post-graduate study tour in Europe and has recommenced practice at his rooms (50 Van Riebeeck Medical Buildings, Schoeman Street, Pretoria).

* * *

Mnr. C. A. R. Schulenburg, F.R.C.S., het van 'n nagraadse studiereis deur Europa teruggekeer en het sy praktyk in sy spreekkamers, Van Riebeeck Mediese Gebou 50, Schoemanstraat, Pretoria, hervat.

Mr. Maurice Arnold, F.R.C.S., formerly of Tower Hill, Johannesburg, has changed his address and is now in practice at 3rd Floor, Clarendon Centre, 4 Park Lane (off Clarendon Circle), Parktown, Johannesburg.

The telephone number remains unchanged (44–7252).

* * *

Dr. G. T. du Toit and Dr. D. Roux (Orthopaedic Surgeons, formerly of 79 de Villiers Street) are now in practice at 3rd Floor, Clarendon Centre Building, Park Lane (off Clarendon Circle), Johannesburg. (Telephones: *Rooms*: 23–1134/5; *Residence*: 44–4378).

BUST OF SIR ALEXANDER FLEMING

PRESENTED TO THE PRETORIA UNIVERSITY MEDICAL SCHOOL

At a well attended ceremony held in the Medical Library of the University of Pretoria Medical School on 23 April 1958, a bust of the late Alexander Fleming (discoverer of penicillin) was presented to the Medical School by Mr. B. E. Bratt, M.P.S., of Pfizer Laboratories South Africa (Pty.) Ltd.

Prof. C. H. Rautenbach, Rector of the University of Pretoria, delivered an address in acknowledgment of this gift, which was received on behalf of the University by Prof. H. W. Snyman, Dean of the Faculty of Medicine.

Prof. Douw G. Steyn, Professor of Pharmacology, also spoke in acknowledgment of the presentation.

From Left to Right. Prof. D. G. Steyn (*Department of Pharmacology*); Prof. C. H. Rautenbach (*Rector*); Mr. B. E. Bratt, M.P.S. (*Pfizer Laboratories*); Prof. J. N. Coetzee (*Department of Micro-biology*) and Prof. H. W. Snyman (*Department of Medicine and Dean of the Faculty of Medicine*).

• • •

Mr. L. J. G. Krüger, M.B., Ch.B., F.R.C.S., has commenced practice as a Specialist Surgeon at 314 Africa House, 3rd Street, Springs.

Telephones: Rooms, 56–6970; Residence, 55–3451.

• • •

Dr. L. Mace David, formerly in practice at 57 Pasteur Chambers, Jeppe Street, Johannesburg, has moved to new rooms, Suite 704, Medical Arts Building, Jeppe Street, Johannesburg. *Telephone* (unchanged): 22–4620.

• • •

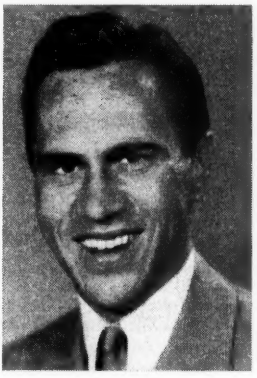
Dr. Michael Malk, formerly in practice at 52 Pasteur Chambers, Jeppe Street, Johannesburg, has moved to new rooms, Suite 704, Medical Arts Building, Jeppe Street, Johannesburg. *Telephone* (unchanged): 22–9659.

• • •

PROF. JOSEPH A. BUCKWALTER

BLOOD GROUPS AND DISEASE

Prof. Joseph A. Buckwalter, Associate Professor of Surgery, University of Iowa, is engaged on a research project jointly sponsored by the Universities of Iowa and Natal and the United States Public Health Service. This work is in progress in the Department of Surgery in the University of Natal and is a continuation of the work which Professor Buckwalter has undertaken over the past 4 years at the University of London with Professor Aird and in his own department.



Prof. J. A. Buckwalter

The investigations conducted so far in Caucasian populations (Europe, America and Australia) have established that an association exists between the ABO blood group of an individual and his susceptibility to certain diseases, e.g. peptic ulcer, gastric cancer, pernicious anaemia, etc.

The work in the Department of Surgery at the University of Natal will continue these studies in African, Indian and White groups and, in addition, control blood group studies will be undertaken on normal samples of these racial groups.

It is anticipated that the results of this project may help to provide decisive answers concerning the nature of the association of blood groups and disease.

Professor Buckwalter's stay in this country will be for a period of 3–4 months, during which time he will visit the University of Cape Town.

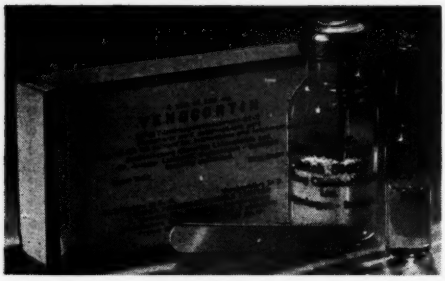
PREPARATE EN TOESTELLE

VENOCORTIN: 'N FOSFORSUUR-ESTER

'N IN WATER OPLOSBARE HIDROKORTISOON-PREPARAAT VIR BINNE-AARSE OF BINNESPIERSE TOEDIENING

By die binne-aarse toediening van kortikoïede is daar opgemerk dat fosfor van die buitesel- na die binnesel-ruimte oorgaan. Ten gevolge van hierdie word daar tans gebruik gemaak van 'n fosforsuur-ester van hidrokortisoon, nl. *Venocortin,* wat 'n vinnige effek het.

Indikasies: Anafilaktiese reaksies, vóór- en náoperasie-skok; ernstige toksisiteit; veral vir akute infeksies; pneumonie; harsingvliesontsteking; die Waterhouse-Friderichsen-sindroom; status asthmaticus; en die voorkoming van skok veral by bejaarde pasiënte.



Let Wel: *Venocortin* is nie bedoel om die plek van enige ander soort algemene behandeling in te neem nie. Dit is 'n waardevolle aanvullende terapie as dit saam met antibiotica, bloed- of ander oortappings, die inaseming van suurstof, ens. gebruik word.

Antibiotiese behandeling moet voortgesit word vir 'n tydperk van ten minste 'n week nadat behandeling met *Venocortin* gestaak is, en die *Venocortin*-behandeling moet beëindig word met korticotrofien, aangesien dit atrofie van die adrenale skors sal voorkom.

Dosis en Toediening: *Venocortin* kan binne-aars of binnespiers toegedien word.

Dosis: *Volwassenes*: 100 mg. *Venocortin* al om die sesde uur, 3–4 maal binne 24 uur.

Suigelinge: 10 mg. *Venocortin* al om die sesde uur, 3–4 maal binne 24 uur.

Kinders van 6 tot 12 Maande: 20 mg. *Venocortin* al om die sesde uur, 3–4 maal binne 24 uur.

Ouer Kinders: 50 mg. *Venocortin* al om die sesde uur, 3–4 maal binne 24 uur.

Suid-Afrikaanse Verspreiders: Protea Pharmaceuticals Ltd., Newtonstraat 7, Wemmer, Johannesburg.

MONDELINGE WYAMINE-SULFAAT VIR NEERSLAGTIGE PASIËNTE

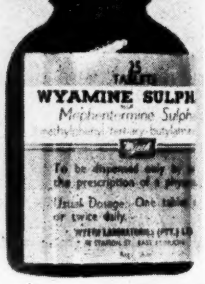
STEMMINGSVERBETERING SONDER OPWINDING

Samestelling: Wyamine is mefentermien (N-metielfeniel-*tersiér*-butielamien).

Iedere *Wyamine*-sulfaat-tablet bevat 25 mg. van die sout.

Farmakologie: Die pressor-effek van *Wyamine* is soortgelyk aan dié van efedrien, maar dit het geen nadelige uitwerking op die hart nie, en dit stimuleer die sentrale senuweestelsel net liggies. In gevalle van duidelike hipotensie sal 25–50 mg. Mondelinge *Wyamine*-sulfaat (1 tot 2 tablette) die sistoliese bloeddruk met 10 tot 25 mm. Hg verhoog, en die diastoliese druk met 5 tot 10 mm. Hg. Normotensiewe en hipertensiewe individue reageer in 'n veel geringer mate op die pressor-effek van *Wyamine*-sulfaat.

Toksisiteit: By die mens het meer as 'n honderd pasiënte wat delikate hartchirurgie ondergaan het, herhaaldelike binne-aarse dosisse van 35 mg. of meer *Wyamine*-sulfaat-inspuiting gekry sonder dat ektopiese ritmes of enige ander onwenslike reaksie hul verskyning gemaak het. Herhaalde dosisse van 35 tot 70 mg. *Wyamine*-sulfaat-inspuiting het geen nadelige effek gehad op pasiënte wat aan akute hartspierinfarkt gely het nie. *Wyamine*-sulfaat word vinnig gemetaboliseer, en daar is geen gevaar van 'n kumulatiewe effek nie.



Uitwerking: Wyamine-sulfaat help om die neerslagtigheid wat alleen of saam met talle siektesindrome verskyn, te verban. As die pasiënt eenmaal van sy gevoelloosheid en uitputting bevry is, is hy in staat om sy vroeëre geestelike en fisiese bedrywigheid te hervat en om weer 'n nuttige lewe te lei. *Wyamine* help om optimisme aan te wakker, en gee die pasiënt 'n opgewekter uitkyk op die lewe en laat hom met 'n gevoel van welsyn.

Voordele in Vergelyking met ander Stemmingsverbeteringsmiddels: Anders as sentrale stimuleermiddels wat met antagonistiese kalmeermiddels verenig moet word om prikkelbaarheid te voorkom, verbeter *Wyamine* in behoorlik gereguleerde dosisse, die stemming sonder om die pasiënt te versteur of te verbyster. Omdat daar geen buitensporige stimulasie is nie, het *Wyamine* nie 'n amfetamien-agtige neerslagtigheidsterugslag nadat die stemmingsverbeteringseffek verdwyn het nie. *Wyamine* het ook geen spesifieke effek op die eetlus nie.

Indikasies: Vir die kroniese moeë, lustelose, sufferige, gevoellose pasiënt met lae bloeddruk; vir stemmingsverbetering in talle neerslagtige toestande, insluitende dié wat kroniese siektes vergesel; oggendmoegheid en kroniese uitputting; die menopause; voor-menstruasie-spanning; die kwale wat met bejaardheid gepaard gaan, en psigogeniese siektes, hardnekkige pyn, hipotensie en narkolepsie.

Dosis: Die gewone dosis is 25 mg. een of twee maal per dag.

Baie pasiënte ondergaan 'n stemmingsverandering gedurende die dag, en is veral neerslagtig in die oggend. In sodanige gevalle is 'n enkele daaglikse dosis van 6.25 tot 25 mg., toegedien in die môre, dikwels voldoende. Die dosis hang af van die reaksie van die pasiënt, en enkele doeltreffende dosisse wissel van 6.25 tot 50 mg. Pasiënte wat meer as een dosis ontvang, moet die finale dosis voor 4-uur nm. neem.

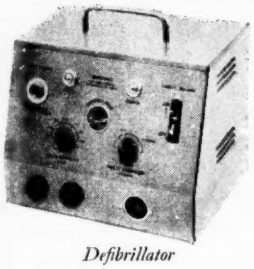
Let Wel: Wyamine het selde enige newe-effekte. 'n Te groot dosis kan dieselfde effek as ander stemmingsverbeteringsmiddels hê (oor-stimulasie, rusteloosheid, slaaploosheid en mislikheid). Geneeshere word aangeraai om versigtig te wees met die behandeling van pasiënte wat aan hoë bloeddruk ly.

Beskikbaarstelling: Bottels van 25 gekeepte tablette.

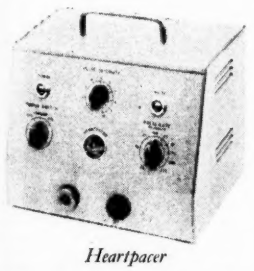
Suid-Afrikaanse Verspreiders: Wyeth Laboratories (Pty.) Limited, Posbus 844, Oos-Londen, en Posbus 8138, Johannesburg.

NUWE APPARAAT VIR ELEKTRIESE BEHANDELING VAN HARTVERSAKING

Twee nuwe eenhede, naamlik die *Defibrillator* en *Heartpacer* word aan die mediese professie aangebied deur Medical Distributors (Eiens.) Bpk. van Johannesburg. Albei hierdie apparate is vervaardig deur die welbekende Birtcher Korporasie van Los Angeles, Kalifornië en word gebruik in talle van die groter sentra in die V.S.A. sedert 1950.



Defibrillator



Heartpacer

Die *Defibrillator* en *Heartpacer* is essensieël vir noodtoestande in enige operasiesaal. Chirurge en geneeshere d w a r s d e u r die wêreld het bewus geword van die waarde van elektriese apparate vir behandeling in gevalle van hartversaking, en daar het 'n merkbare vermindering gekom in die aantal sterfgevalle as gevolg van die gebruik van hierdie nuwe apparate.

Die *Defibrillator* word direk op die hartkamers gebruik deur 'n snit in die b o r s w a n d. Die funksie van die apparaat is om die hartkloppings te koördineer wanneer trilling plaasvind. Met die ontwerp van hierdie apparaat was veiligheid van die pasiënt die oorwegende faktor en 'n outomatiese stroombreker is aangebring waardeur verhoed word dat die hartspiere beskadig word deur 'n elektriese brand indien te veel stroom deurdring.

Die *Heartpacer* word gebruik as 'n elektriese stimulant wat van buite af aangewend word wanneer die hart stadig of onreëlmatig klop. Elektrodes word op die borswand geplaas en die masjien word in werking gestel. Die *Heartpacer* kan onmiddellik gebruik word wanneer die hart ophou om te klop met dien verstande dat daar geen ventrikulêre trilling is nie. Nadat ventrikulêre trilling met die *Defibrillator* behandel is (indien nodig) kan die *Heartpacer* vir etlike ure, dae of selfs maande toegepas word totdat die normale hartklop terugkeer.

Wetenskaplike Literatuur en Verdere Informasie van hierdie Moderne Apparate is Verkrygbaar van die Uniale Verspreiders:

Medical Distributors (Eiens.) Bpk., Posbus 3378, Johannesburg.

STREPTO-PENICILLIN NOVO

Strepto-Penicillin Novo is 'n waterige suspensie, gereed vir gebruik. Dit bevat dihidrostreptomisiensulfaat en penisillienprokaïen-G, sowel as suspensie- en dispersiemiddels.

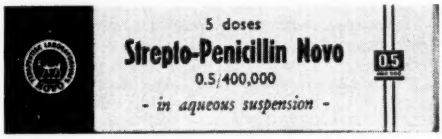
Een dosis (2 ml.) *Strepto-Penicillin Novo* bevat:

Dihidrostreptomisiensulfaat	0.5 g. basis
Penisillienprokaïen-G	400,000 i.e.

Gesamentlike terapie met penisillien en streptomisien is van waarde by die behandeling van gemengde infeksies veroorsaak deur sowel Grampositiewe as Gram-negatiewe bakterieë, want die 2 antibiotica het 'n addisie-effek. Die gesamentlike bakteriologiese spektrum van penisillien en streptomisien dek die meeste van die patogeniese mikroorganismes wat 'n geneèsheer in sy algemene praktyk teëkom, en daar moet in gedagte gehou word dat hierdie samestelling 'n inspuitbare preparaat beskikbaar stel wat in die meeste gevalle toegedien kan word as daar kontra-indikasies vir die gebruik van ander breë-spektrum-antibiotica is weens hipersensitiwiteit of newe-effekte in die spysverteringskanaal.

Temeer, daar is vasgestel dat daar 'n sinergistiese werking tussen penisillien en streptomisien is, veral in gevalle waar die infeksie-mikro-organisme vir albei antibiotica gevoelig is. Gesamentlike preparate word derhalwe aangedui veral vir die behandeling van siektes wat gekenmerk word deur gemengde infeksies (infeksies van die urinêre stelsel, buikvliesontsteking, brongitis, ens.), sowel as infeksies wat nie op penisillienterapie reageer nie.

Preparate van hierdie aard kan ensiemvernietiging van die penisillien voorkom, want streptomisien is doeltreffend teen die meeste penisillinase-produserende bakterieë, bv. stafilokokki. Daarbenewens word die gevaar van weerstandskragtigheid verminder deur die gelyktydige toediening van penisillien en streptomisien.



Strepto-Penicillin Novo moet alleen binnespiers ingespuit word, en die geneesheer moet die nodige voorsorgsmaatreëls tref om te voorkom dat die naald 'n bloedvat binnedring.

In die geval van herhaalde inspuitings moet 'n ander inspuitingsplek elke slag gekies word om die moontlike gevaar van pyn te verminder. 'n Plaaslike verdowingsmiddel kan by die suspensie gevoeg word.

As die spuit wat gebruik is in gekonsentreerde alkohol gebêre word, kan die suier vassit weens die afsaksel van streptomisien. Derhalwe word geneeshere aangeraai om die spuit met steriele water uit te spoel voor en na gebruik.

Spuite en naalde kan egter in 'n 70% oplossing van alkohol gebêre word, maar dan moet die geneeshere sorg dat hulle so leeg as moontlik is voordat hy hulle gebruik.

Alleenverspreiders vir Suid-Afrika: Pan African Pharmaceuticals (Pty.) Ltd., Posbus 10340, Telefoon: 44-8594, Johannesburg.

COSCOPIN

VIR DOELTREFFENDE HOESBESTRYDING

Die aktiewe bestanddeel in *Coscopin* is noskapien wat vroeër as narkotien bekend gestaan het. Noskapien is 'n opium-derivaat, maar chemies of farmakologies is dit nie verwant aan morfien nie. Dit het 'n kragtige, spesifieke sedatiewe effek op die hoesrefleks. Dit is so aktief soos kodeïen vir die bestryding van hoes, maar anders as kodeïen is dit 'n ligte lugpypverwyder en asemhalingsopwekmiddel, en dit veroorsaak geen hardlywigheid nie. Dit het geen pynstillende, euforiese of narkotiese effek nie.

Coscopin word aangedui vir die verligting van hoes wat aan 'n verskeidenheid van oorsake, insluitende brongitis en infeksies van die boonste asemhalingskanaal, na-influensa-prikkeling en neoplasme te wyte is. Weens sy geringe lugpypverwydingseffek en die stimulerende uitwerking wat dit op die asemhalingsentrum het, is *Coscopin* ook van besondere waarde vir die behandeling van toestande soos asmatiese brongitis en kinkhoes waar daar kontra-indikasies is vir die gebruik van middels soos kodeïen wat die lugpype vernou.

Coscopin is verkrygbaar in 2 vorms—as 'n smaaklike, kersie-gegeurde stroop, en as tabletjies. *Coscopin*-stroop word te koop aangebied in bottels van 4 vlocistof-ons, bevattende 12.5 mg. noskapien per dragme. Elke *Coscopin*-tablet bevat 25 mg. noskapien, en word verpak in dosies van 20.

Die aanbevole dosis is:

Volwassenes: Twee teelepelsvol stroop of een tablet al om die 2–3 uur.

Kinders: 5 tot 14 jaar—die helfte van die dosis vir volwassenes. Ouer as 14—die dosis vir volwassenes.

Coscopin-stroop moet onverdun geneem word. Die tablet moet toegelaat word om stadig in die mond op te los.

Evans Medical Supplies, Posbus 6607, Johannesburg.

‚MAREZINE'-INSPUITING

VIR ERNSTIGE, DOELLOSE BRAKING

Burroughs Wellcome & Co. (S.A.) Ltd. kondig die beskikbaarstelling aan van *‚Marezine'*-inspuiting, 'n soort siklisienlaktaat, om die reeds gevestigde mondelinge brakingsbestrydingsmiddel, *‚Marzine'*-tablette, 'n soort siklisienchloried, aan te vul. Iedere ampul van 1 k.s. bevat 50 mg. van die aktiewe bestanddeel vir binnespierse inspuiting.

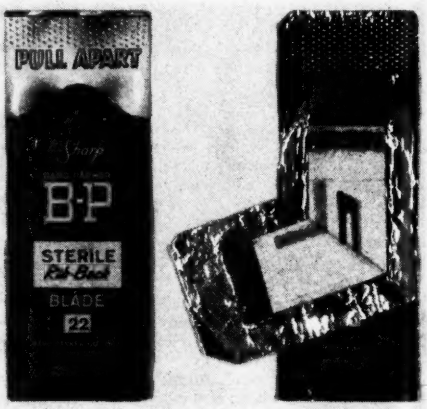
Die nuwe produk word aangedui vir die behandeling van ernstige, doellose mislikheid en braking wanneer die mondelinge roete nie gebruik kan word nie of ongeskik geag word. Dit word ook aangedui wanneer 'n vinnige effek verlang word. *‚Marezine'* het reeds die bewys gelewer dat dit besonder waardevol is vir die voorkoming van na-operasie-mislikheid en -braking. In sulke gevalle kan 50 mg. (1 k.s.) binnespiers toegedien word saam met die na-operasie-geneesmiddels, of twintig tot dertig minute voor die verwagte einde van die operasie. Daar kan ook verwag word dat *‚Marezine'* hoogs doeltreffend sal wees by die behandeling van ernstige braking tydens swangerskap.

Die *British Medical Journal* (22 Maart 1958, bl. 675 *et seq.*) sê dat die mees algemene newe-effek van morfien nie die deprimering van die asemhaling is nie, maar wel mislikheid en braking wat egter ‚geheel en al gekontroleer kan word deur die gebruik van siklisienchloried.'

STERIELE ‚B-P-RIB-BACK-LEM'

Die nuwe steriele *B-P-Rib-Back-lem* word in 'n lekvrye pakkie beskikbaar gestel.

Die koevert wat maklik oopgemaak kan word, kan, indien verlang, in 'n stoomsterilisator behandel word.



Die *Rib-Back-lem* binne in die koevert is *steriel*, en kan uit die koevert uit aan die handvatsel bevestig word sonder dat dit nodig is om die lem self aan te raak.

Hierdie lemme word gemaak van koolstofstaal, die beste materiaal vir die skerp snykant wat die chirurg nodig het.

Die nuwe verpakking verseker maksimum-veiligheid, gerief tydens die operasie, en chirurgiese doeltreffendheid.

Suid-Afrikaanse Agente: Gurr Surgical Instruments (Pty.) Ltd., Posbus 1562, Johannesburg.

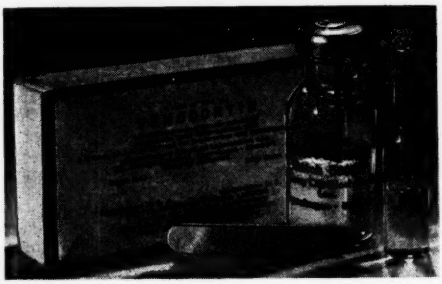
PREPARATIONS AND APPLIANCES

VENOCORTIN: A PHOSPHORIC ACID ESTER

A WATER-SOLUBLE HYDROCORTISONE PREPARATION FOR INTRAVENOUS AND INTRAMUSCULAR ADMINISTRATION

In the intravenous administration of corticoids it has been observed that phosphorus is transported from the extra-cellular to the intra-cellular space. This suggested the use of a phosphoric acid ester of hydrocortisone, viz. *Venocortin,* which will produce rapid effects.

Indications: Anaphylactic reactions, pre- and post-operative shock, severe intoxication, especially in acute infections, pneumonia, meningitis, Waterhouse-Friderichsen's syndrome, status asthmaticus and prevention of shock especially in the case of elderly patients.



Note: *Venocortin* does not supplant any other form of general treatment. It is a valuable supplementary therapy in conjunction with antibiotics, blood or other transfusions, oxygen inhalation, etc.

Antibiotic treatment should be continued for at least one week after *Venocortin* treatment has been discontinued and the course of *Venocortin* treatment should be concluded with corticotrophin as this will prevent atrophy of the adrenal cortex.

Dosage and Administration: *Venocortin* can be given intravenously or intramuscularly.

Dosage: *Adults*: 100 mg. of *Venocortin* every sixth hour, 3–4 times in 24 hours.

Infants: 10 mg. of *Venocortin* every sixth hour, 3–4 times in 24 hours.

Children from 6 to 12 months: 20 mg. of *Venocortin* every sixth hour, 3–4 times in 24 hours.

Older Children: 50 mg. of *Venocortin* every sixth hour, 3–4 times in 24 hours.

South African Distributors: Protea Pharmaceuticals Limited, 7 Newton Street, Wemmer, Johannesburg.

ORAL WYAMINE SULPHATE FOR DEPRESSED PATIENTS

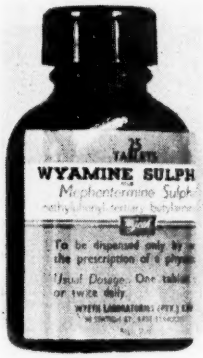
MOOD AMELIORATION WITHOUT EXCITATION

Composition: Wyamine is mephentermine (N-methyl-phenyl-*tertiary*-butylamine).

Each *Wyamine* Sulphate tablet contains 25 mg. of the salt.

Pharmacology: Wyamine approximates the pressor action of ephedrine without adversely affecting the heart, and mildly stimulates the central nervous system. In frank hypotension, 25–50 mg. (1 to 2 tablets) Oral *Wyamine* Sulphate increases systolic blood pressure by 10 to 25 mm. Hg and diastolic pressure by 5 to 10 mm. Hg. Normotensive and hypertensive individuals respond to a much lesser degree to the pressor effects of *Wyamine* Sulphate.

Toxicity: In Man, over 100 patients undergoing delicate cardiac surgery have received repeated intravenous doses of 35 mg. or more of Injection *Wyamine* Sulphate without developing ectopic rhythms or any other undesirable reactions. Repeated doses of 35 to 70 mg. Injection *Wyamine* Sulphate did not produce any ill effects in cases with acute myocardial infarction. *Wyamine* Sulphate is rapidly metabolized, with no danger of cumulative effects.



Action: Wyamine Sulphate helps dispel depression occurring alone or in conjunction with many disease sydromes. With the lifting of apathy and fatigue, the patient becomes more capable of former mental and physical activity, and may return to former usefulness. *Wyamine* helps revive optimism, leaving the patient with a brightened outlook and a sense of well-being.

Advantages Over Other Mood-Ameliorating Drugs: Unlike central stimulants which must be combined with antagonistic sedatives to avoid irritability, *Wyamine,* in properly regulated doses, smoothly elevates the mood without disturbing or distracting the patient. Because of lack of excessive stimulation, *Wyamine* does not have an amphetamine-like 'rebound' of depression when the mood-uplifting effect has worn off. *Wyamine* has no specific effect on appetite.

Indications: For the chronically tired, listless, lethargic, apathetic patient with low blood pressure; for mood amelioration in many depressive states, including those accompanying chronic disease, morning tiredness and chronic fatigue, the menopause, premenstrual tension, pregnancy, old age and psychogenic ailments, persistent pain, hypotension and narcolepsy.

Dosage: The usual dosage is 25 mg. once or twice daily.

Many patients experience a diurnal variation in mood, being most depressed in the morning. In such cases, a single daily dose of 6.25 to 25 mg., given in the morning, is often sufficient. Dosage depends on the response of the patient, the single effective dose ranging from 6.25 to 50 mg. Patients on multiple doses should take the final dose before 4 p.m.

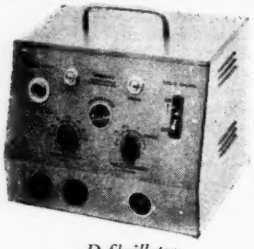
Note: Wyamine rarely produces side effects. Overdosage may produce the same effects (overstimulation, restlessness, insomnia and nausea) as other mood-ameliorating drugs. Caution is advised in the treatment of hypertensive patients.

Supplied: Tablets: Bottles of 25 scored tablets.

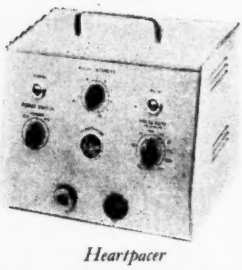
South African Distributors: Wyeth Laboratories (Pty.) Limited, P.O. Box 844, East London and P.O. Box 8138, Johannesburg.

NEW APPARATUS FOR THE ELECTRICAL TREATMENT OF CARDIAC FAILURE

Two new units, the *Defibrillator* and *Heartpacer* are presented to the medical profession of Southern Africa by Medical Distributors (Pty.) Ltd., of Johannesburg. This apparatus has been developed by the well-known Birtcher Corporation of Los Angeles, California, and has been in use at many of the larger centres in the U.S.A. since 1950.



Defibrillator



Heartpacer

The *Defibrillator* and *Heartpacer* are essential stand-by items in any operating theatre. Surgeons and physicians throughout the world have become familiar with the use and value of electrical apparatus for the treatment of cardiac failure and there has been an appreciable decrease in the death rate as the result of the use of these modern appliances.

The *Defibrillator* is used directly on the ventricles through an incision in the chest wall. Its function is to co-ordinate the human heart beat when fibrillation has occurred. Safety to the patient has been the guiding factor in the design of this apparatus, which is fitted with an automatic circuit breaker, so as to prevent electrical burning of the heart muscle, which might result from excessive amperage or voltage.

The *Heartpacer* is an electric stimulator which is used externally to restore the heart beat when it is slow or faltering. Electrodes are placed on the chest wall and the machine put into operation. The *Heartpacer* may be used immediately the heart fails, provided there is no ventricular fibrillation, or after this has been arrested by the *Defibrillator*, and may be maintained for many hours, days or even months, until the normal beat recurs.

Scientific Literature and Further Information about Both these Units may be Obtained from the Sole Agents:

Medical Distributors (Pty.) Ltd., P.O. Box 3378, Johannesburg.

STREPTO-PENICILLIN NOVO

Strepto-Penicillin Novo is a ready-for-use aqueous suspension containing dihydrostreptomycin sulphate, penicillin-procaine-G, as well as suspending and dispersing agents.

One dose (2 ml.) of *Strepto-Penicillin Novo* contains:

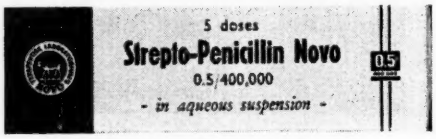
Dihydrostreptomycin sulphate	0.5 g. base
Penicillin-Procaine-G	400,000 i.u.

Combined therapy with penicillin and streptomycin is of value in mixed infections caused by both gram-positive and gram-negative bacteria on account of the additive effect of the 2 antibiotics. The combined bacteriological spectrum of penicillin and streptomycin covers most of the pathogenic micro-organisms encountered in general practice, and it should be remembered that this combination makes available an injectable preparation which, in the majority of cases, can be used when other broad-spectrum antibiotics are contra-indicated due to hypersensitivity or side effects in the gastro-intestinal tract.

Moreover, synergistic action betwen penicillin and streptomycin has been established, particularly in cases where the infecting micro-organism is sensitive to both antibiotics.

Combined preparations are therefore indicated, especially in diseases characterized by mixed infections (urinary tract infections, peritonitis, bronchitis, etc.), besides infections which have not responded to penicillin therapy.

Preparations of this type can prevent enzymatic destruction of the penicillin as streptomycin is effective against most penicillinase-producing bacteria, e.g. staphylococci. In addition, the simultaneous administration of penicillin and streptomycin reduces the risk of resistance.



Strepto-Penicillin Novo should only be injected intramuscularly and the usual care should be taken to ensure that the needle has not entered a blood vessel.

In case of repeated injections, the site of injection should be changed every time, in order to reduce possible pain. A local anaesthetic may be added to the suspension.

If the syringe used has been kept in concentrated alcohol, the piston may become fixed owing to precipitation of streptomycin; therefore rinse the syringe in sterile water before and after use.

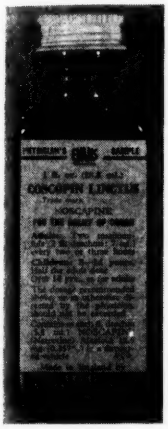
Syringes and needles, etc. may, however, be kept in 70% alcohol when care is taken to empty them as thoroughly as possible before use.

Sole South African Distributors: Pan Africa Pharmaceuticals (Pty.) Ltd., P.O. Box 10340, Telephone: 44-8594, Johannesburg.

COSCOPIN

FOR EFFECTIVE CONTROL OF COUGH

The active ingredient of *Coscopin* is noscapine, formerly known as narcotine. Noscapine is an opium derivative but is not related chemically or pharmacologically to morphine. It has a powerful specific depressant action on the cough reflex. It is as active as codeine in the suppression of cough but, unlike codeine, it is a mild bronchodilator and respiratory stimulant and is non-constipating. It has no analgesic, euphoric or narcotic effect.



Coscopin is indicated for the relief of cough due to a variety of causes including bronchitis and infections of the upper respiratory tract, post-influenzal irritation and neoplasm. Because of its mild bronchodilating action and its stimulating effect on the respiratory centre, *Coscopin* is also of particular value in conditions such as asthmatic bronchitis and whooping cough, where the use of broncho-constricting drugs such as codeine is contra-indicated.

Coscopin is available in 2 forms, as a palatable cherry-flavoured Linctus and as Lozenges. *Coscopin* Linctus is packed in bottles of 4 fl. oz. containing 12.5 mg. of noscapine per drachm. *Coscopin* Lozenges each contain 25 mg. noscapine and are packed in cartons of 20.

The recommended dosage is:

Adults: Two teaspoonfuls of linctus or one lozenge every 2–3 hours.

Children: For 5 to 14 years—half the adult dose. Over 14 years—as for adults.

Coscopin Linctus should be given undiluted; the Lozenges should be allowed to dissolve slowly in the mouth.

Evans Medical Supplies, P.O. Box 6607, Johannesburg.

'MAREZINE' INJECTION

FOR SEVERE, PURPOSELESS VOMITING

Burroughs Wellcome & Co. (S.A.) Ltd. announce the introduction of *'Marezine'* Brand Cyclizine Lactate Injection to supplement the already established oral anti-emetic *'Marzine'* brand Cyclizine Chloride tablets. Each 1 c.c. ampoule contains 50 mg. of the active principle for intramuscular injection.

The new product is indicated for the treatment of severe, purposeless nausea and vomiting when the oral route cannot be used or is considered unsuitable. It is also indicated when a rapid onset of action is desired. *'Marezine'* has proved especially valuable in the prevention of post-operative nausea and vomiting, when 50 mg. (1 c.c.) intramuscularly may be given with the pre-operative medication or twenty to thirty minutes before the expected termination of surgery.

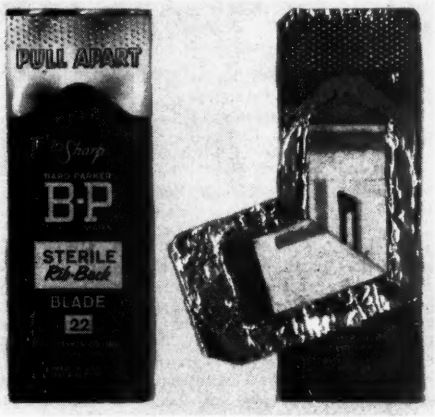
'Marezine' may also be expected to be highly effective in severe cases of vomiting during pregnancy.

The *British Medical Journal* (22 March, 1958 pp. 675 *et seq.*) observes that the most frequent side-effect of morphine is not respiratory depression but nausea and vomiting, which may be 'completely controlled by the use of cyclizine chloride.'

B-P STERILE RIB-BACK BLADE

The new *B-P Sterile Rib-Back Blade* is presented in a puncture proof package.

The envelope, which opens easily, can be autoclaved if desired.



The *Rib-Back Blade* inside the envelope is *sterile*, and may be affixed to the handle from the open envelope without the blade itself being touched.

These blades are made of carbon steel, which is the best for the fine cutting edge required by the surgeon.

The new pack provides maximum safety, operating convenience and surgical efficiency.

South African Agents: Gurr Surgical Instruments (Pty.) Ltd., P.O. Box 1562, Johannesburg.

REVIEWS OF BOOKS

POLYMYOSITIS

Polymyositis. By John N. Walton, M.D., M.R.C.P. and Raymond D. Adams, M.D. 1958. (Pp. 256 + Index. With Figs. 32s. 6d.). Edinburgh: E. & S. Livingstone Ltd.

This monograph begins with a synopsis and a critical review of a wide variety of diseases affecting muscle, but distinct from the syndromes associated with progressive muscular dystrophy. The muscle diseases—polymyositis—are divided into 4 groups:

1. Polymyositis—acute with myoglobinuria, subacute or chronic.
2. Polymyositis with muscular weakness as the dominant feature but with evidence of an associated collagen disease, or dermatomyositis with minimal skin changes.

3. Severe collagen disease with minor muscle involvement or dermatomyositis with florid skin changes and muscular disability of secondary importance.

4. Polymyositis or dematomyositis associated with malignant disease.

The remarkable variability of the clinical picture is well illustrated in the *Appendix*, which contains the case reports of 40 cases personally observed by the authors. Separate chapters on the investigations, natural history and prognosis of the different groups are further adjuncts in the separation of this wide variety of clinical patterns. The chapter on the pathological aspects is extensive and the finer details of the similarities and differences in the 4 groups are well documented. The histological features of the muscle sections are well reproduced.

In the final chapter the diagnoses made at various stages of the illness in the cases of the authors' series of 40 cases are recorded. The common mistaken diagnoses were muscular dystrophy, myasthenia gravis and disseminated lupus.

Drs. Walton and Adams have made a considerable attempt to separate the wide variety of clinical syndromes of unknown etiology associated with polymyositis. Clinicians and pathologists interested in muscle disease will benefit from a careful study of this monograph.

GASTROENTEROLOGICAL CYTODIAGNOSIS

Atlas of Gastroenterological Cytodiagnosis (German and English Text). By Prof. N. Henning and Dr. S. Witte. English translation by Dr. R. O. K. Schade. 1957. Pp. 104. DM 38. Germany: Georg Thieme Verlag.

The term 'cytological diagnosis' has become associated almost exclusively with the study of the female genital tract and the lungs. Certainly there has been considerable justification for this in the great publicity which the American literature, in particular, has given to these fields, and to all the methods and interpretations which have been associated with the name of Papanicolaou, although in recent years American workers have been applying cytodiagnostic methods to other areas of the body. In various centres in Europe, however, considerable attention has been paid to cytodiagnosis of lesions in the alimentary tract since the end of the last war and this is one of the first publications in book form defining this work. In Germany, in particular, Professor Henning and Dr. Witte, of the University of Erlangen, have developed techniques (both of sampling and of staining) which will prove of great diagnostic value in experienced hands. Comparison of their cytological findings with extensive histological biopsy material has enabled the authors to place their interpretations on safe foundations. They were successful in differentiating normal mucosa from gastritic mucosa and, indeed, were able to diagnose atrophic gastritis by the finding of goblet cells. By the application of fluorescent and intravital staining methods, they succeeded easily in separating tumour cells from other elements as a screening procedure. Although their stomach findings depended on new techniques, examination of duodenal contents, bile duct contents, and other regions were based upon conventional methods of sampling.

The present monograph, which contains both German and English texts in parallel translation, consists of 45 pages of text and 58 pages of superb photomicrographs. These illustrate normal and atypical cells as observed by the various techniques of microscopy which have been employed. The authors are to be congratulated on their choice of black-and-white photographs in this atlas rather than the coloured photomicrographs or drawings which have rendered other atlases artistically more impressive, often at the expense of precise practical value.

The English text (translated by Dr. Schade of the University of Durham) is didactic and it errs, if anything, in its strict objectivity. However, this makes it the more surprising to note the occasional dogmatic statement about the nature of an individual cell even though supported by photographs. It is also surprising to note the adoption by these authors of Papanicolaou's unnecessarily equivocal subdivision of cytological diagnosis into 5 categories rather than the 3 adopted by more sceptical workers who prefer to regard desquamated cells as either 'positive,' 'negative' or 'suspicious,' in respect of malignancy.

This monograph will be welcomed by all pathologists confronted occasionally with these extremely difficult diagnostic problems. The technical production is of a high standard, but a firmer and more durable cover, for what must inevitably be a 'bench' book, would be an advantage. This is a desirable amendment which could be incorporated in the next edition.

CUNNINGHAM'S PRACTICAL ANATOMY

Cunningham's Manual of Practical Anatomy. Revised by James Couper Brash. Volume III. 1958. (Pp. 500 + Index. With Figs. 28s.). 12th ed. London: Oxford University Press.

It is 10 years since the previous edition of this dissecting manual was issued. As a guide to the student, its position remains unchallenged and pre-eminent. The order of dissection has been changed, however, the sequence no longer being based upon the body being placed in the lithotomy position.

There is a clarity about the print and the illustrations which makes the volume attractive to read—an important psychological consideration for the undergraduate student.

For the main part, English equivalents of the Paris Nomenclature (approved by the International Anatomical Congress in 1955) have been used in the new edition. Some of the more familiar BR terms have been retained and, where important changes have been introduced, the equivalent term in the Paris Nomenclature is given in brackets. The index, however, is sufficiently comprehensive to solve any terminological problem for the reader. It will clearly take a very considerable time before unanimity is achieved about the descriptive terms, e.g. 'brachiocephalic artery' has logic on its side but will not readily be equated with 'innominate artery.'

In conformity with the preceding volume, Vol. 3 is bound in a new waterproof material which means that, if the book becomes soiled in the dissecting room, it can easily be cleaned by sponging with soap and water.

The extremely reasonable price (almost a miracle of publishing achievement in these times) should ensure that no student will have any difficulty about acquiring this invaluable textbook.